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TUBERCULOSIS OF THE ENDOMETRIUM*

BY

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From the David Elder Infirmary, Glasgow

IT is only in the past 10 or 15 years that it has become generally appreciated that unsuspected endometrial tuberculosis, often unaccompanied by any palpable pelvic lesion, is a relatively common condition. In view of the present world-wide interest in this subject, it is perhaps fitting that this lecture should follow the admirable discourse by Mr. Tom Barns (1955) on the natural history of pelvic tuberculosis. William Blair-Bell did not number pelvic tuberculosis among his many known interests, but I have no doubt that he would have been keenly interested in recent developments had he been alive today.

In recent years, there has been a widespread awakening of interest in the whole subject of genital tuberculosis in women and particularly in endometrial tuberculosis. It is now generally realized that this condition is much more frequent than was previously thought and it is likely that this is due in great part to the routine use of endometrial biopsy or diagnostic curettage in patients with infertility, irregular uterine bleeding or amenorrhoea.

EARLY LITERATURE

I shall now refer briefly to the early literature on tuberculosis of the uterus. The first recorded case of this condition was reported by Morgagni (1762) when he described caseation in the uterus and tubes in a girl aged 20 years, who had died of tuberculous peritonitis. Since then many papers have been published dealing partly or wholly with uterine tuberculosis and among the most notable of these are contributions by Williams (1894), Berkeley (1903), Murphy (1903, 1904), Norris (1921), Greenberg (1924), Daniel (1925) and Jameson (1935). An extensive review of the literature is given by each of these authors.

INCIDENCE

Very varied views have been expressed on the question of the incidence of endometrial tuberculosis. In an attempt to clarify this point, I have studied the matter from a number of aspects and the results are shown in Table I. The first aspect is from the accumulated histological material of a gynaecological hospital. Some years ago (Sutherland, 1943), I made a study of the histological preparations of the Pathological Department of the Royal Samaritan Hospital for Women, Glasgow, over a period of 7 years. During this time 5,521 curettings and 864 uterine specimens were examined histologically. Tuberculosis of the endometrium was found in the curettings 61 times (1·1 per cent) and in the uterine specimens 12 times (1·4 per cent). In this paper the few comparable figures are reviewed and these are in reasonable agreement with my own.

The next aspect is from the clinical records of a gynaecological hospital. In association with my colleague Doctor Garrey (Sutherland and Garrey, 1951), I made a study of the clinical records of the Royal Samaritan Hospital for Women, Glasgow, during a 20-year period. During this time 65,943 patients were admitted

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TABLE I

The Percentage Incidence of Tuberculosis of the Endometrium in Glasgow

In the histological material of a gynaecological hospital	1·1
In the clinical records of a gynaecological hospital	0·27
In infertility	5·6
In "functional uterine bleeding" between puberty and the menopause	1·0
In "functional uterine bleeding" in young women	4·0
In "organic uterine bleeding"	0·9
In post-menopausal bleeding	0·1

to the hospital and histologically-proved genital tuberculosis of various types was discovered in 369 instances (0·56 per cent). Comparison with published figures from gynaecological hospitals in various parts of the world showed similar results.

Tuberculosis of the endometrium was found in 178 cases, representing 48·19 per cent of cases of genital tuberculosis and 0·27 per cent of all admissions to the hospital. The incidence of endometrial tuberculosis was more than three times as high in the second 10-year period as in the first. It is probable that this increase is due in great part to the more extensive use of endometrial examination in various conditions, particularly infertility, in the more recent cases.

Next, I should like to consider the incidence of tuberculosis of the endometrium in infertility. During a 20-year period ending on 31st December, 1954, Sharman (1955a) investigated 3,804 cases of primary infertility in the Royal Samaritan Hospital for Women, Glasgow. In all of these patients endometrial biopsy or curettage was carried out, endometrial tuberculosis being found in 216 (5·6 per cent).

In recent years, many similar though usually much smaller series have been published throughout the world. The figures are too numerous to present here in detail but extensive reviews on this matter have been published by Sharman (1952) and by Schaefer (1953). The figures reported vary considerably and many are appreciably higher than the 5·6 per cent found by Sharman (1955a). There is certainly nothing in these figures or in the others quoted previously to suggest that genital tuberculosis in women is unusually frequent in the West of Scotland.

There is, however, one country in which this condition is certainly uncommon and that is Australia. Grant and Mackey (1953) found only one example of endometrial tuberculosis in 600 infertility patients investigated in Sydney before the last war. Recently they reported that the incidence is on the increase and has risen to 1 in 240 cases. They consider that this increase is largely found in the refugee or immigrant population from Europe and say that the combination of a patient with an unpronounceable name, infertility and damaged tubes is a signal for a full investigation for pelvic tuberculosis. They wonder, for a new and developing race, whether it is not as important that the new female immigrant be screened for pelvic tuberculosis as for the pulmonary lesion.

Lastly, I should like to discuss the incidence of endometrial tuberculosis in various types of abnormal uterine bleeding. I have investigated this aspect in four groups of cases. The first of these is functional uterine bleeding occurring between puberty and the menopause. I analyzed the endometrial histology in 1,000 cases of abnormal uterine bleeding occurring in the absence of gross pelvic pathology (Sutherland, 1949), all types of abortion and all patients with bleeding after the menopause being excluded. Tuberculosis of the endometrium was found on 10 occasions (1 per cent).

The second is abnormal uterine bleeding in young patients. I made a study of the endometrial histology in 200 cases of abnormal uterine bleeding occurring in women aged 20 years or under (Sutherland, 1953). Endometrial tuberculosis was found in 8 cases (4 per cent). I consider that this incidence constitutes a clear-cut indication for curettage in such patients, all other considerations apart. A number of writers advise against curettage in cases of supposed functional bleeding in young women because they consider that this procedure is

unnecessary or because of the risk of psychological disturbance following the operation. In a fairly extensive experience of this procedure, I have never known the slightest harm result to any patient and most of the writers who advise against it do so with little or no factual evidence to support their view.

The third group comprises cases of uterine bleeding with a possible organic pelvic cause. I studied the histology of the endometrium in 1,000 cases of abnormal uterine bleeding occurring in association with gross pelvic disease which might explain it (Sutherland, 1950a). All patients with post-menopausal bleeding and all types of abortion were excluded from this series. Tuberculosis of the endometrium was found 9 times (0·9 per cent).

The fourth group consists of cases of post-menopausal bleeding. In conjunction with my colleague Doctor McBride, I recently made a study of 1,000 cases of post-menopausal bleeding, special attention being paid to the histology of the endometrium (Sutherland and McBride, 1954). Tuberculosis of the endometrium was only found once (0·1 per cent). This patient was aged 46 years and had had a natural menopause 19 years previously. The findings in this group of cases are in agreement with the general view that endometrial tuberculosis is rarely encountered after the menopause. This matter is considered by Jameson (1935) and by Towers (1954), both of whom review the scanty literature on the subject.

Clinical Aspects

The present series consists of 200 cases of this condition which have been investigated in Glasgow during the past 5 years. A few of these patients were encountered in the routine working of my own unit and a considerably larger number were referred to me from other gynaecological departments and chest clinics throughout the West of Scotland.

Some of these cases form part of an investigation into the results of the treatment of tuberculosis of the endometrium. This investigation is being conducted in various centres throughout the country by a Joint Subcommittee representing the Royal College of Obstetricians and Gynaecologists and the Research Committee of the British Tuberculosis Association.

During the past 5 years, I have held a weekly clinic in my own hospital, devoted entirely to genital tuberculosis in women. In the initial stages, the number of patients attending was small, but today the average weekly attendance is about 10 patients. The vast majority of the patients attending have proved endometrial tuberculosis, although I am glad to investigate and treat women with suspected or proved genital tuberculosis of all types.

Previous health. I should next like to discuss certain relevant clinical aspects of the 200 cases at present under review. The first is the previous general health. A careful enquiry was made into the previous history of all cases, particularly in relation to earlier extra-genital tuberculous lesions. A history of definite or possible extra-genital tuberculosis was obtained in 111 of the 200 patients and details of these illnesses are shown in Table II. It will be seen that the total number of lesions is 135, in view of the fact that multiple conditions had been present in quite a number of the cases. The interval between the earlier tuberculous manifestations and the discovery of the endometrial infection varied widely, but in the majority it was 5 years or more.

In the Table, patients with a previous history of pleurisy are separated from the other categories. In this connexion a difficulty arose which is encountered by most people who undertake an enquiry of this type. This was to decide how much significance should be attached

Table II

History of Previous Extra-Genital Tuberculosis—111 Cases

Abdominal tuberculosis, usually proved at laparotomy	58
Pulmonary tuberculosis	20
Bone and joint tuberculosis	9
Renal tuberculosis	1
Pleurisy	47

to a previous history of pleurisy as distinct from pleurisy with effusion. True dry pleurisy is not infrequently due to the tubercle bacillus, but unfortunately "pleurisy" is one of the most abused terms in medicine and is often applied to conditions in which there is no inflammation of the pleura and in which the only feature in common with true pleurisy is pain in the chest. Pleural effusion was present in many of my patients in this group but by no means in all, and I can only assume that the condition may have been tuberculous in the remainder.

It is known that both the human and the bovine strains of the tubercle bacillus can cause genital tuberculosis in women. In view of this it was decided to investigate the possibility of a relationship between genital infection due to the bovine strain and the place of residence of the individual up to the age of 15 years. The assumption was that the source of the bovine infection was probably milk and that an individual living in a strictly rural community would be more likely to contract such an infection from an unpasteurized milk supply than would be an urban resident. This line of investigation proved of little value, as the tubercle bacillus was found to be of the human type in every case in which it was identified. This aspect will be considered in some detail in a later section.

Age incidence. With reference to the age incidence, the average age of my patients was 28 years at the first attendance, the youngest patient being 16 years and the oldest 48.

TABLE III
Previous Obstetrical History—23 Patients

1 previous full-time pregnancy	7
2 previous full-time pregnancies	5
1 previous abortion	4
3 previous full-time pregnancies	3
9 previous full-time pregnancies	1
2 previous full-time pregnancies and 1 abortion	1
2 previous abortions	1
1 previous tubal pregnancy (in a tuberculous tube)	1

Obstetrical history. Twenty-three patients were unmarried. Among the remaining 177, only 23 gave a history of previous pregnancy. The details of these pregnancies are shown in Table III. This low incidence of fertility in cases of tuberculosis of the endometrium is now widely recognized and a considerable volume of literature has accumulated on this subject.

In a previous paper I drew attention to the fact that the development, or at least the discovery, of a chronic form of endometrial tuberculosis in the post-partum period is by no means uncommon (Sutherland, 1952). In the present series there are no less than 9 cases (4·5 per cent) in which the tuberculous lesion probably developed during pregnancy, or in the post-partum period. These patients usually complained either of bleeding or of abdominal pain dating from childbirth or miscarriage.

Diagnostic curettage revealed endometrial tuberculosis in each case and I consider that this condition should be kept in mind when investigating patients with similar histories. The interval between delivery or miscarriage and discovery of the endometrial condition varied considerably in my 9 patients, but it was not more than 4 months in the majority. In one instance, curettage was carried out for incomplete abortion and the curettings were found to consist of products of conception and fragments of endometrium showing tuberculous infection.

The literature on post-partum genital tuberculosis is scanty and most of the cases described previously were acute in onset, widespread and fatal. The literature is reviewed in my own paper (Sutherland, 1952) and in the recent communications by Donaldson (1952) and by Morrison and Ealand (1954). One post-partum case is reported by Donaldson (1952) and 2 by Morrison and Ealand (1954), who state that 24 such cases have been described since 1940.

Menstrual history. With reference to menstrual history, while the majority of the patients had a normal menstrual cycle, a considerable number reported profuse and sometimes irregular bleeding. The occurrence of amenorrhoea in a relatively small number emphasizes the present view that this symptom is much less frequent than many earlier publications indicated.

Symptomatology. The principal symptoms are shown in Table IV. In the time available, it will not be possible to discuss the symptomatology of these cases in any detail and I shall confine my attention to the principal complaint in each case. *Infertility* was the most common symptom

TABLE IV
Principal Symptoms—200 Cases

Infertility	77
Abdominal pain	45
Profuse and sometimes irregular bleeding	33
Amenorrhoea, usually secondary	22
Vaginal discharge	10
No complaint	13

and this finding is in keeping with most recent work on this subject. The volume of literature on the relationship between endometrial tuberculosis and infertility is very considerable and it would be quite impossible to discuss it in any detail at present. The literature on this matter is fully reviewed in papers by Sharman (1952), Schaefer (1953) and Studdiford (1955) and in a previous communication of my own (Sutherland, 1950b).

Pain was also a common symptom, varying in character and degree and situated in the lower abdomen. The next complaint in order of frequency was *abnormal uterine bleeding*, usually rhythmic but sometimes irregular and occurring several times in patients under 20 years of age. Of the 22 patients with *amenorrhoea*, only 2 were of primary type and the remainder were secondary. While working in a gynaecological endocrine clinic, on several occasions I have encountered patients with primary amenorrhoea and normal secondary sex characters, who subsequently were found to have endometrial tuberculosis. The futility of employing hormone therapy without preliminary diagnostic curettage in such patients is obvious.

Ten patients complained only of *vaginal discharge* and the existence of unsuspected endometrial tuberculosis was revealed by curettage. In most of these cases, however, there was either cervical or vaginal infection sufficient to explain the discharge, which cleared up after treatment of the local condition. My own impression is that vaginal discharge is not a characteristic symptom of endometrial tuberculosis. Thirteen patients made no complaint of any kind when they were referred to me, but invariably gave a history of some previous tuberculous infection, usually abdominal and detected at laparotomy.

General examination. A thorough general examination was carried out in all cases. Each patient was seen by a chest physician and the chest and abdomen were X-rayed. X-ray examination of the chest revealed 7 unsuspected active pulmonary lesions and 79 healed pulmonary lesions. X-ray examination of the abdomen showed calcified glands in 24 instances. A catheter specimen of urine was taken for guinea-pig inoculation in each case. Out of 196 results so far received, 6 were positive and the remainder were negative.

An interesting point in connexion with these results is that they revealed evidence of hitherto unsuspected extra-genital tuberculous lesions in no less than 50 patients with no history of such conditions. Twenty-four of these patients had a healed pulmonary lesion, 2 had an active pulmonary lesion, 21 had calcified glands in the abdomen and 3 had an active renal lesion. These findings are not surprising, however, because it is well known that many tuberculous lesions, especially primary ones, may remain silent or undiagnosed.

If the 2 methods of investigation are combined, namely the history of previous extra-genital tuberculous lesions on the one hand and radiological or bacteriological evidence of them on the other, 161 (80·5 per cent) of the 200 cases at present under review were found to have had at least one previous extra-genital tuberculous lesion. These results may be compared with those recently reported by Barns (1955) who found evidence of extra-genital tuberculosis in 73 per cent of 107 patients with genital tuberculosis.

Other routine tests included full blood examination, Kahn test, blood sedimentation and Mantoux test. Blood examination was normal apart from an occasional example of mild microcytic anaemia, the Kahn test was always negative, blood sedimentation was variable but within normal limits in the majority, and the Mantoux test was always positive.

Pelvic examination. The findings on pelvic examination are shown in Table V. As a number of patients had multiple lesions, the total number is seen to exceed 200. It has been my practice to carry out cervical biopsy in all patients with suspected or proved endometrial

TABLE V
Findings on Pelvic Examination—200 Cases

Adnexal swelling, usually bilateral	88
Retroversion of uterus	31
Erosion of cervix	24
Cystic enlargement of one ovary	7
Uterine fibroids	3
Pyometra	1
No palpable abnormality	71

tuberculosis and cervical erosion. In the present series, unsuspected cervical tuberculosis was discovered on 4 occasions in this way. These results would suggest that it is worth while carrying out this procedure in such cases and that the incidence of cervical tuberculosis may be higher than is generally supposed at present.

Tubal insufflation. In the course of the initial investigation of the majority of the infertility cases, tubal insufflation was carried out. Out of 77 patients complaining primarily of infertility, tubal insufflation was performed in 72 and the tubes were found to be blocked in 47 of these (65 per cent). This figure is in close agreement with that recently reported by Sharman (1955b), who found tubal blockage in 62·7 per cent of 185 cases of primary infertility with endometrial tuberculosis. Estimates in the literature as to the incidence of tubal blockage in infertility cases in general vary greatly, but are usually very much below the figure of 65 per cent encountered in the present series. For example, Sharman (1955a) found tubal blockage in approximately 20 per cent of over 4,000 primary infertility cases.

DIAGNOSIS

A provisional diagnosis of endometrial tuberculosis was based initially on the histological findings in the curettings in most cases, although in a few the histological appearances were inconclusive or negative and bacteriological confirmation was awaited. Bacteriological proof was sought in the vast majority and I shall discuss the results later. Vaginal swabs were also taken in all but 9 of the cases in an attempt to identify the tubercle bacillus. Positive results were obtained in only 12 cases and the remaining 179 were negative. It would thus appear that the routine taking of vaginal swabs for diagnostic purposes is not justifiable.

HISTOLOGY

In the vast majority of the cases, the histological appearances were similar. The picture was one of infrequent and usually isolated small tubercles, scattered irregularly through the endometrium. Occasionally a cluster of tubercles could be seen in a single microscopic field. In most cases, however, the lesions were scanty and careful search through a slide of all the endometrium removed in a thorough curettage sometimes revealed only a single tuberculous focus, most of the fragments appearing absolutely normal. In most cases the tuberculous foci occurred mainly towards the surface of the endometrium, but in a few instances, particularly when they were fairly frequent, they were seen at all levels.

The individual tuberculous lesions are quite characteristic. A central zone of epithelioid cells is always present and usually, though not invariably, one or more giant cells can be seen. A small central area of caseation is sometimes present and the focus is usually surrounded by a zone of lymphocytic infiltration. The glandular structure in the endometrium does not show any abnormality, apart from the glands in the immediate vicinity of the tuberculous lesions. In many cases the stroma is infiltrated throughout with lymphocytes and plasma cells in moderate numbers, and in an occasional specimen this chronic inflammatory reaction is very marked. The histological picture is that usually described as miliary tuberculosis of the endometrium.

On measurement the average size of the tubercles was found to be 0·21 mm., the smallest measuring 0·14 mm. and the largest 0·33 mm. The true average size of the tuberculous foci is probably much larger than 0·21 mm., however, as serial sections were not obtained, and it is almost certain that in many instances the section did not pass through the centre of the tubercle. Even in a single piece of endometrium the size of the tubercles was found to vary considerably. It is not possible to say whether this variation was due to a true difference in size or merely to the cutting of the lesions at different levels.

In a small number of specimens the appearances were different from those described, the curettings being composed mainly or entirely of tuberculous granulation tissue. Many authors have described the histological appearances in tuberculosis of the endometrium, though few have done so in much detail. A full description is given in two recent papers by Haines (1951, 1952). In general, the reports are in agreement with those found in my own cases.

Bacteriology

Bacteriological proof of the tuberculous nature of the lesion was sought in 185 of the cases and a positive result has so far been obtained in 141. The routine adopted in the examination of specimens was that each specimen of endometrium was divided into two equal parts, one of which was prepared for histological examination and the other for injection into guinea-pigs and inoculation of culture media. The media used for direct inoculation with endometrium were Löwenstein-Jensen and Dubos-Davies. Where a positive result was obtained on Löwenstein-Jensen medium either by direct inoculation or from positive guinea-pigs, the sensitivity of the organism to various drugs was tested on Dubos-Davies medium. Typing of the organism was carried out by inoculation of rabbits. I think that it is likely that the very small amount of tissue obtained by curettage in many instances may be the main reason for the rather high number of negative results.

In all cases with positive bacteriology, an attempt was made to type the organism. This was successful in 120 instances, the tubercle bacilli invariably being of the human type. Similar results were obtained by Barns (1955) who found that all his cases of pelvic tuberculosis in which culture was successful were due to the human type of bacillus. Cases of endometrial tuberculosis due to the bovine variety of tubercle bacillus are rare but examples have been reported. In the recently published preliminary report of the Joint Sub-committee on the treatment of tuberculous endometritis with streptomycin and PAS (Sutherland, 1954), the organism was identified in 56 cases, 4 being of the bovine type.

The resistance of the organism to various drugs was tested and the results are shown in Table VI. Sensitivity to streptomycin was tested in all possible cases and sensitivity to INH was a routine procedure in the later cases. Sensitivity to PAS was only estimated in one instance when specially requested. A number of sensitivity results are still awaited in the most recent cases in the series. All sensitivity tests were carried out according to the methods described in the Medical Research Council trials relating to pulmonary tuberculosis.

Table VI

Sensitivity of Organisms to Various Drugs

Streptomycin-sensitive	103
Streptomycin-sensitive (partial)	7
Streptomycin-resistant	9
INH-sensitive	36
INH-resistant	2
PAS-sensitive	1
PAS-resistant	0

Control Cases

I shall next refer to the management of these patients and shall begin by considering the control group. Thirty-eight of the earlier cases in the present series were initially allocated to a control group, as they formed part of an investigation into the efficacy of streptomycin and PAS in the treatment of endometrial tuberculosis. Reference has already been made to this trial, which was conducted in a number of centres throughout the country. When this trial was being planned, it was decided that the best way to ascertain the value of the drugs concerned would be in the form of a controlled trial. At that time, previous experience did not suggest that to withhold treatment was likely to involve any appreciable risk to the patient in most cases.

It was accordingly agreed to include control cases, under the following conditions:

(1) All control patients whose disease was still active at the end of an observation period of one year should receive a full course of treatment.

(2) All control cases showing any clinical deterioration should be withdrawn from the trial and treated at once.

(3) All cases in which it was felt that it might be harmful to withhold treatment should be excluded from the trial and treated at once.
(4) No patients with active extra-genital tuberculous lesions should be included in the trial.

During the year of observation in this group, no active treatment of any kind was carried out. These patients were kept under observation and reported regularly, endometrial biopsy being carried out at intervals of 3 months when possible. The results in the control group of cases are shown in Table VII. It will be seen from this Table that 30 patients (78·9 per cent) were either positive at the end of the control year or later, or required treatment before the end of the control year because of clinical deterioration. Five patients defaulted during the control year and in only 3 was the endometrium consistently negative at the end of the control year and subsequently. It is thus apparent that the vast majority of patients with endometrial tuberculosis who do not receive drug treatment do not undergo spontaneous cure.

TABLE VII

Results in "Control" Group—38 Cases

(Percentages in brackets)

Positive at end of year	21	(55)
Required treatment during year	7	(18)
Negative at end of year, but later positive ..	2	(5)
Defaulted during year	5	(13)
Negative at end of year and subsequently ..	3	(8)

The patients in whom the condition persisted or recurred will be considered further in a later section. There were 7 patients who required treatment during the control year, 5 with a flare-up of the tuberculous condition in the pelvis, 1 with tuberculous meningitis and 1 with a reactivation of a healed pulmonary lesion. Of the 2 patients whose endometrium was negative after 1 year but later became positive, in 1 the condition recurred for the first time after 4-years observation. The 3 patients whose endometrium has remained negative throughout may be examples of spontaneous healing or of cure following curettage. Much attention to these two matters has been paid by some early writers but their standards of cure are often unsatisfactory.

TREATMENT

Some doubt has been expressed as to the advisability of treating patients with tuberculosis of the endometrium unless bacteriological proof has been obtained. My own view is that I am prepared to treat such patients on the basis of the histological findings only and it is my regular practice to do so, without awaiting the bacteriological results. There were 59 patients (29·5 per cent) in whom the tubercle bacillus has not so far been found, although in 15 of these bacteriological proof was not sought initially for various reasons. In 36 of these 59 patients there was either a previous history of an extra-genital tuberculous lesion or evidence of such a lesion was discovered by X-ray examination of the chest or abdomen.

The histological appearances in those cases lacking bacteriological proof are identical with those in the remainder and I have no doubt that they are true examples of endometrial tuberculosis. As I have mentioned before, I am convinced that the quantity of endometrium obtained plays a considerable part in this matter. It is a constant finding that in histologically-positive cases in which ample endometrium is obtained for guinea-pig inoculation and culture, the results are almost invariably positive. On the other hand, where the amount of tissue is small, there is an appreciable risk of getting a negative bacteriological result although the histology is positive. Another aspect of this problem is the fact that the disease in the endometrium is essentially focal in character in the vast majority of cases. In some specimens of endometrium, the lesions are very scanty and it may well be that no tubercles are present in the tissue used for guinea-pig inoculation or culture.

With reference to the methods of treatment employed, surgery has not been used in any of my cases to date, although the possibility of employing it is being kept in mind. It is possible that I shall resort to surgery in an occasional drug-resistant patient and I shall have no hesitation in operating on any patient who has distressing symptoms which fail to respond to drug treatment. The question of the place of surgery in pelvic tuberculosis has been discussed by numerous authors. Most recent writers agree with the views expressed by Stallworthy at the

British Congress of Obstetrics and Gynaecology in 1952. He considers that surgery should be avoided except in menopausal or post-menopausal patients without activity elsewhere, or where adnexal masses develop or increase despite other measures, where uterine bleeding associated with uterine infection delays recovery, or where fistulas fail to heal. He also stresses the fact that if surgery is to be used at all, it must be radical.

A great deal has been written in recent years on the treatment of genital tuberculosis with various drugs, particularly streptomycin and PAS. It would be quite impossible for me to review these papers in any detail today, but I should like to make special mention of the excellent contributions from Sweden, particularly those by Jedberg (1950), Liljedahl and Rydén (1950) and Rydén (1953). Most writers are now agreed that endometrial tuberculosis should be treated, irrespective of the presence or absence of symptoms. Stallworthy (1952) has stated that genital tuberculosis, whether suspected or not, is a serious disease, and I am in entire agreement with this view. The vast majority of writers on this subject have obtained good results in the treatment of endometrial tuberculosis with various drug combinations, though in many series the numbers of cases are small.

Various schedules of drug treatment were employed in my own cases, depending on circumstances. Treatment was almost always given on an out-patient basis except for a small group of patients who had a pelvic spread of the disease following the initial curettage. These patients were admitted to hospital as emergencies and the earlier part of the drug schedule was administered there. It was usually possible to discharge them after 2 or 3 weeks, the remaining treatment being given to them as out-patients. Most of the patients received treatment either at the out-patient department of my own hospital or from their own doctors. They were ambulant throughout and many continued in their jobs. In no instance was it considered necessary to admit these patients to sanatoria, except in a few cases with extra-genital spread of the tuberculous process.

Drug treatment was used in 192 of my 200 patients. Of the remaining 8, all in the control group, 3 remained negative at follow-up and 5 defaulted during the control year. The treated patients can be divided into 3 categories.

(1) *Streptomycin and PAS.* The course given in the earlier cases in this category was 1 gramme of the calcium chloride complex of streptomycin daily for 84 consecutive days, with 3 grammes of the sodium salt of PAS 4 times daily over the same period. In the later cases, streptomycin sulphate was substituted for the calcium chloride complex and the daily dosage of PAS was increased to 20 grammes. Including 25 control patients requiring treatment, 137 cases were treated with streptomycin and PAS, the last 48 being on the second schedule.

An attempt has been made to keep all treated patients under observation indefinitely although in many instances this has not proved feasible. During the first year following the commencement of treatment, the condition has been observed by endometrial biopsy, usually carried out every 3 months in the premenstrual phase of the menstrual cycle. This procedure was almost always performed at the out-patient department and general anaesthesia was only used in the occasional patient who was admitted to hospital for 1 or 2 days for this purpose.

At the end of the first year of follow-up, admission for full curettage under general anaesthesia was arranged, and subsequent control was conducted entirely by endometrial biopsy at intervals of 6 to 12 months. A good deal has been said and written on the risks of endometrial biopsy and of dilatation and curettage in patients with endometrial tuberculosis. My own experience is that full curettage is definitely risky in the untreated patient and that an occasional pelvic flare-up inevitably occurs following the initial curettage in patients in whom endometrial tuberculosis is unsuspected. Even in treated cases, I think that it is unwise to carry out full curettage unless there have been at least 2 consecutive negative endometrial biopsies previously.

Endometrial biopsy is certainly less risky than full curettage and I have had no trouble after using it in treated cases, provided that it is carried out gently and carefully by an experienced person. Despite every care, however,

endometrial biopsy was occasionally followed by pelvic flare-up in the control cases and I do not now consider that further work with controls is justified. The only reason for using full curettage in suspected cases of endometrial tuberculosis is that it yields a larger amount of tissue than endometrial biopsy and thus the chance of discovering tubercle bacilli, if present, is increased.

The results are shown in Table VIII. It will be seen from this Table that 95 patients (69 per cent), had a persistently negative endometrium following treatment, the average duration of the follow-up being 19 months; 27 (19 per cent) had recurrence of the endometrial infection and most of these received additional treatment of one kind or another. The average time after treatment at which recurrence was diagnosed was 16 months and these cases will be considered further in a later section. The remaining 15 patients (12 per cent) had no follow-up, some failing to complete treatment and others defaulting at the end of treatment.

TABLE VIII
Results of Treatment with Streptomycin and PAS
137 Cases
(Percentages in brackets)

Cases remaining negative after treatment ..	95	(69)
Cases recurring after treatment	27	(19)
Cases without follow-up	15	(12)

(2) *Streptomycin and INH.* The combination of streptomycin and INH was used in 53 further patients, 5 of whom were previously controls. The dosage employed was 1 gramme of streptomycin sulphate daily for 84 consecutive days, combined with 100 milligrammes of INH twice daily over the same period. The results are shown in Table IX. It will be seen that 43 cases (81 per cent) have so far remained negative after treatment, the average duration of follow-up being 12 months. It is not possible to say that the results obtained with streptomycin and INH are better than those obtained with streptomycin and PAS, as the latter group were followed up for a longer average time and a number of the recurrences were in the second and third years after treatment.

TABLE IX
Results of Treatment with Streptomycin and INH
53 Cases
(Percentages in brackets)

Cases remaining negative after treatment ..	43	(81)
Cases recurring after treatment	4	(8)
Cases without follow-up	6	(11)

(3) *INH alone.* The remaining 2 patients were treated with INH alone. One was admitted to a sanatorium following a pelvic flare-up and I have no follow-up for her. The other patient had already had full treatment with streptomycin and PAS in another hospital and was given INH, 50 milligrammes twice daily for 84 consecutive days. Her endometrium has remained negative for 20 months following this treatment. Although this patient, and several others about to be mentioned, received INH alone, it is now generally agreed that the use of a single drug is undesirable, and this method has consequently been abandoned.

Recurrent cases. There were 31 cases showing recurrence of the endometrial infection following initial treatment with one or other of the drug combinations. Various additional lines of treatment were adopted in these cases. The earlier patients received INH, in doses of 50, and latterly 100, milligrammes twice daily for 84 days. Some time ago the use of INH alone was abandoned and two drugs in combination were employed instead. The exact drug combination used varied with the individual case and with the sensitivity of the organism, but recently I have usually employed PAS and INH. The results are shown in Table X. It will be seen that a substantial number of patients remained negative after a second course of

TABLE X
Results in Cases with Recurrence after First Course of Treatment—31 Cases

Cured after second course	12
Second course in progress	10
Second course refused	2
Positive after second course	3
Positive after second course, attending for third course	2
Cured after third course	1
Positive after third course, attending for fourth course	1

treatment, the average time of follow-up in these cases being 15 months. In only a small number has a second course so far proved ineffective, although quite a few are still in progress.

Drug reactions. Toxic drug reactions occurred in a disturbingly large number of my patients and treatment had to be stopped before the end of the course in no less than 26 of the 192 patients treated (14 per cent). Streptomycin was the drug responsible in 21 of these, vestibular disturbance occurring 17 times and skin rashes in the other 4. In one of the latter cases the generalized skin eruption was very severe and there was loss of most of the hair from the scalp. The total dosage of streptomycin administered before the onset of the toxic symptoms varied between 11 and 60 grammes. The 5 remaining toxic reactions were due to PAS, each patient having a severe generalized upset, although the symptoms varied with the individual. All the patients in this group had some gastro-intestinal disturbance and 2 had a skin eruption. The total dosage of PAS before onset of these symptoms varied between 147 and 1,300 grammes.

Although treatment had to be discontinued in all 26 patients, no permanent ill-effects of any kind were observed. Even the patient who lost most of her hair improved rapidly after cessation of treatment and her hair has now returned to normal. In the more recent cases, a change was made from the calcium chloride complex of streptomycin to streptomycin sulphate in the hope that this would reduce the incidence of toxic manifestations. Unfortunately, this has not proved to be the case, although painful injections are much less frequent with the latter preparation. In addition to the cases just described, minor upsets occurred in an appreciable number but in these the full course was completed, sometimes after a spell in hospital for desensitizing. No untoward effects of any kind have so far been observed with INH.

Symptomatic results. I should now like to discuss the results of treatment in relation to symptomatology. The commonest presenting symptom was infertility, which was present 77 times. One patient had a 3-months miscarriage after diagnosis of the endometrial condition but before treatment was instituted. No patient had a normal pregnancy following treatment, but one had a ruptured tubal pregnancy. While these results are disappointing, they are not at all surprising. Examples of pregnancy occurring in patients with a history of proved endometrial tuberculosis are rare in the literature, although several cases have been reported recently. It is likely that the low fertility of these patients is related to the high incidence of blockage or morbidity of the Fallopian tubes. While treatment may arrest the active infection, the disorganization of tubal structure, which had already occurred, may be such that normal function cannot be restored.

The results of treatment in relation to the remaining complaints were generally satisfactory. Of the 45 patients complaining mainly of abdominal pain, 37 reported after treatment. Thirty-two were completely free of pain, 4 were considerably improved, and only 1 reported no change in her complaint. The effect of treatment on the adnexal masses was very varied. In many cases the swellings were no longer palpable, and in many others they were considerably reduced in size. In a few patients, however, there was no apparent change in these masses.

It is highly probable, though not certain, that the majority at least of these adnexal masses were tuberculous in nature. It is not usually possible without laparotomy to obtain accurate information regarding the response of associated adnexal masses to treatment, and I can only speculate as to how many of them clear up along with the endometrial infection. The 4 patients with associated cervical tuberculosis all had complete healing of the cervical lesion following treatment, as shown by cervical biopsy, and by examination with a speculum.

Thirty-three patients complained of profuse and sometimes irregular bleeding. Of 28 patients in this group who attended after treatment, all reported a return to a normal menstrual cycle. The results in the amenorrhoea cases were also satisfactory; of the 22 patients with amenorrhoea 18 attended after treatment. Twelve of these patients reported restoration of normal menstruation, including 1 patient aged 24 with primary amenorrhoea. No change was reported by the 6 remaining patients, 2 of whom were over 40 years of age.

Discussion

When considering the results of treatment of endometrial tuberculosis with various drug combinations, it is apparent that the results so far obtained are considerably better than those observed in the controls. It is too early to assess the value of streptomycin and PAS as compared with streptomycin and INH, though the results to date suggest that the latter combination is at least as effective as the other, and is less likely to be associated with toxic drug reactions. The occurrence of major toxic drug reactions in 26 patients is disturbing, and I hope that new drugs will become available in the near future which will reduce the risk of such upsets.

Although a few control cases did become negative without treatment, I consider that the results that I have presented show that it is not now justifiable to withhold treatment from any patient with proved tuberculosis of the endometrium. The main reasons for this conclusion are the fact that most of the control cases remained positive at follow-up and the fact that an appreciable number showed clinical deterioration in the course of the control year and required immediate treatment. In addition, the majority of the treated cases have so far remained negative and most patients have been cured of their principal complaints apart from those with infertility. It is my intention to continue to follow-up these patients as long as they can be persuaded to attend, and it is quite possible that certain of my conclusions may be modified in the light of further experience.

Acknowledgments

I should like to pay a tribute to the many colleagues and friends who have helped to make this work possible. In particular, I should like to express my thanks to the gynaecologists and chest physicians throughout the West of Scotland who have referred most of my cases to me, to Doctor Govan and Mr. Fraser of the Research Department of the Glasgow Royal Maternity and Women's Hospital, who have undertaken all the histological and bacteriological work, to Doctor Cuthbert and Doctor Garrey, who have been associated with this work from the start, to my Registrars, Donald Bruce and Kenneth Greig, for their untiring help and to the nursing staff of the David Elder Infirmary, Glasgow.

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TWO CASES OF PROVED ENDOMETRIAL TUBERCULOSIS FOLLOWED BY SUCCESSFUL PREGNANCY

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A CASE of full-time pregnancy after proved endometrial tuberculosis has recently been recorded by Hallum and Thomas (1955) who also reviewed the literature. Their case had been treated with streptomycin and para-amino salicylic acid (PAS). The 2 cases described here had received similar treatment, and we consider that they are also worthy of record.

Case 1

Mrs. E., born 15th April, 1923, first reported to the gynaecological clinic on 27th September, 1951, complaining of infertility. She had then been married 6 years, contraception having been practised for the first 4 years. She stated that she had had congestion of the lungs at the age of 15, but no abnormality was now detected on examination.

On vaginal examination, no pelvic abnormality could be detected, and she was advised to have her husband examined before she herself had an insufflation. The husband's examination and seminal analysis were entirely satisfactory. Insufflation as an out-patient procedure was unsuccessful, and the patient was admitted for insufflation and endometrial biopsy on 12th January, 1952, when tubal patency was proved at 180 mm. mercury.

The histological report revealed tuberculous endometritis.

Radiological examination of the chest showed no evidence of a pulmonary tuberculous focus.

Treatment was immediately commenced with injections of streptomycin 1 g. daily and PAS, under the supervision of her own doctor.

She was re-admitted for dilatation and curettage on 28th March, 1952, and no tubercles were seen on histology. However, the patient failed to conceive and she was re-admitted for further curettage and insufflation on 25th August, 1952. Insufflation on this occasion failed to demonstrate tubal patency, but once again no tubercles were seen on histology, and guinea pig inoculations were subsequently reported negative.

A hysterosalpingogram was performed on 21st November, 1952. This demonstrated that the right Fallopian tube was patent with adjacent pocketing, suggestive of adhesions, and that the left tube filled but was irregular in outline and slightly dilated towards its free extremity, with doubtful spill.

The patient was advised to attend again in one year if she had not conceived, when the question of adoption would be discussed. But she wrote on 11th January, 1954, stating that she had not conceived and that she was making the necessary plans for adoption. However, we were pleased to hear from her again on 27th March, 1955, announcing that she had not proceeded with the adoption plans because she had indeed become pregnant, and that a female infant weighing 5 pounds 12 ounces had been born on 11th February, 1955.

Case 2

Mrs. W. was aged 27 when she was first seen in 1950. Her complaint was of irregular and excessive menstrual periods for 2 years.

She had had pneumonia at the age of 18, followed by a pleural effusion. Radiological confirmation of the effusion showed no evidence of pulmonary tuberculosis. Thereafter she had developed a cough, which was still present.

In 1947 she had had a normal delivery at term.

When seen in 1950, pelvic examination revealed no obvious abnormality, and a diagnosis of dysfunctional uterine haemorrhage was made, for which she was admitted for dilatation and curettage, but no curettings were obtained, even though the last menstrual period had commenced 3 weeks previously. Radiological examination of the chest at this time showed no sign of tuberculosis, but revealed minor bronchiectatic areas in the right lung.

When she was seen at the follow-up clinic, it was found that her complaints were unchanged, and continued thus despite oxytocics and sedatives for the next year.

In 1951 it was found that she had a right-sided ovarian cyst and she was admitted for operation. At laparotomy a large follicular cyst of the right ovary was enucleated. The uterus, both Fallopian tubes and the left ovary appeared normal. The patient made an uninterrupted recovery from this operation and did not attend the follow-up clinic for a further 18 months, at which time she still complained of irregular and excessive periods. It was now decided to re-admit her for a further diagnostic curettage and the possibility of tuberculosis was considered.

This operation was performed in October, 1953, when a normal sized anteverted mobile uterus with some thickening of the right Fallopian tube was felt. The macroscopically normal curettings obtained were sent for histological examination, guinea pig inoculation and cultured for *Mycobacterium tuberculosis*. The histological examination and guinea pig inoculation both proved negative, but the culture produced a growth of acid-alcohol fast organisms typical of *Myco. tuberculosis*, first seen after 27 days incubation. This culture was inoculated into a further guinea pig which showed typical tuberculous lesions when killed 4 weeks later. Radiological examination of the chest was repeated revealing no change from that found 3 years before. No acid fast bacilli could be demonstrated in the urine. The erythrocyte sedimentation rate was 13·5 mm. in one hour and the haemoglobin was 72 per cent.

In December, 1953 a course of streptomycin, 1 g. intramuscularly daily, together with PAS 4 g. four times daily, was commenced under the supervision of her own doctor and the district nurse. The course lasted for 3 months, until a total of 90 g. streptomycin and 1,440 g. PAS had been given.

In March, 1954, the patient was re-admitted for a repeat curettage, when she stated that her menstrual periods were now normal. Examination under anaesthesia revealed no pelvic abnormality, the thickening of the right Fallopian tube being no longer palpable. Normal looking curettings obtained on the 22nd day of her cycle revealed no evidence of tuberculosis on histological examination, guinea pig inoculation, nor on culture.

When seen a few months later, the patient's condition remained satisfactory, and a hysterosalpingogram was performed. The uterine cavity and both Fallopian tubes were seen to outline normally with the ready passage of the neohydriol into the peritoneal cavity.

She again omitted to attend the follow-up clinic until February, 1955, when she returned complaining of 7-weeks amenorrhoea. She was thought to have an early pregnancy and this indeed proved to be true.

She attended the antenatal clinic regularly and uneventfully, feeling well throughout. A further radiological examination of the chest showed no change in the bronchiectasis, whilst similar examination of the foetus revealed no abnormality.

On 10th September, 1955, 10 days before term, she was admitted in labour. The obstetrical situation was satisfactory, but she did complain of pain in the right side of the chest, pleuritic in nature, which had been present for a day or so. The temperature was 99·4° F. with a pulse rate of 92 beats per minute. Physical examination of the chest revealed only scattered râles, heard mainly over the right lung base. A diagnosis of

an acute exacerbation of the bronchiectasis was made, and a specimen of sputum was sent for laboratory examination. Treatment was then commenced with soluble Penicillin, 500,000 units intramuscularly, 6-hourly, for 5 days.

Later the same day, after being in labour for 6 hours, she had a normal delivery of a living male infant weighing 7 pounds 5 ounces. The placenta was sent for histological examination, guinea pig inoculation and cultured for *Myco. tuberculosis*, but the reports of these tests, when received later, all showed no evidence of tuberculosis.

The temperature and pulse returned to normal within 24 hours, whilst the chest pain disappeared in 48 hours. Radiological examination of the chest showed no change from the earlier films. The laboratory report on the sputum taken during labour showed numerous pus cells and mainly Gram-positive cocci, whilst the culture revealed a profuse growth of normal flora. She continued to make satisfactory progress on Penicillin and postural drainage.

Breast feeding was suppressed in the puerperium and mother and child were discharged fit on the 15th day. During the puerperium, investigation of the renal tract, chest and abdomen revealed no evidence of a primary tuberculous focus.

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A SUGGESTION FOR A CYTOLOGICAL TEST OF CANCER-CURE

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IN the course of routine cytological screening of gynaecological patients carried out in the Hammersmith Hospital it was observed that the vast majority of women suffering from cancer of the uterus exhibited high cornification indices in their vaginal smears. The cornification index (i.e., the percentage of superficial squamous cells with pyknotic nuclei) and the number of superficial squamous cells, were regarded as manifestations of the patient's oestrogen level for the following reasons: (1) normally ovulating women reach a peak value of cornification index at ovulation (de Allende and Orias, 1950; Pundel, 1950; Wachtel and Plester, 1954), and (2) oestrogen administration to normal postmenopausal women raises the cornification index and changes the pattern of the smear profoundly; the number of basal cells decreases, superficial squames appear and there is an appreciable rise in the percentage of cornified cells (de Allende and Orias, 1950; Pundel, 1950).

The cornification index is estimated by counting the percentage of cells with pyknotic nuclei among 200 unselected superficial and intermediate squames. The basal cells are omitted from this count.

In non-treated post-menopausal women not suffering from malignant disease, granulosa cell tumours, endometrial hyperplasia, etc., the cornification indices range below 5 and are usually 0. The pattern of their vaginal smears is atrophic, i.e., the smears are largely composed of basal cells.

Single cytological estimations of oestrogen levels in pre-menopausal women suffering from cancer of the uterus are of no diagnostic help as there is a great individual variation in different normal women and the same patients may even show different peak values in different cycles. The observation of high cornification indices in post-menopausal cancer patients is much more significant. In our own material, of 38 unselected cancer patients past the menopause in whom the cornification indices were recorded, 32 or 84·2 per cent had a C.I. over 10, some of them reaching values between 50 and 70. This increase in the number of cornified cells occurred with equal frequency in squamous cancers and adenocarcinomata.

This association between malignant growths of the uterus and an abnormally high cornification index in the absence of functioning ovarian tissue suggested a connexion between the two and the idea of investigating the cornification indices in treated cancer patients was tempting.

The results of this investigation, despite the relatively small number of patients examined in this way, are striking enough to warrant publication at this early stage in the hope of encouraging other workers in the field to repeat and extend these investigations. The cornification indices and appearances of vaginal smears in women with other tumours, especially cancers of the breast, would be of great interest.

Twenty-seven patients who had received treatment for cancer of the uterus within the past 5 years were followed up cytologically. It appeared that a high cornification index following treatment of malignant uterine disease, be it by radical hysterectomy or full doses of radiotherapy, was an indication of persistence of malignancy.

Of 10 patients who had received extensive treatment for uterine carcinoma in the past 5 years (6 of them had full radiotherapy and 4 radical hysterectomy) with clinical, histological and cytological recurrence or persistence of malignant disease, 9 had persistently high

cornification indices and only 1 had a C.I. of 10 which was regarded as inconclusive. Four of these 10 patients were suffering from adenocarcinoma and 6 had squamous malignancies. Seventeen cancer follow-up patients without evidence of recurrent or persisting disease all had cornification indices below 5.

If the finding of a high cornification index after treatment of malignant disease indicates, as suggested, the continued presence of carcinoma and is reproducible on a larger number of patients, this would indeed provide a simple test, involving very little skill, for detection of residual or recurrent disease.

Discussion

We believe that the cornification index in vaginal smears, first described by Allen (1924), mirrors the oestrogen level, although it is, at present, not established whether other substances might produce a similar, oestrogen-like effect. Assuming that the substances responsible for the high cornification index in smears of carcinoma patients are, in fact, oestrogens, the question of the source of these hormones invites interesting speculation.

One can argue that full X-ray doses and even super-voltage treatment by the linear accelerator do not completely destroy ovarian function, but this argument does not hold in patients after surgical removal of the ovaries. Other possible sources of oestrogen production are the adrenal glands and the tumour itself. The adrenals normally contribute a small fraction to the total circulating oestrogens and it may be postulated that castration, i.e., deprivation of the main oestrogen-producing source, leads to either direct or indirect (*via* the pituitary) stimulation of the adrenals. If this were the case, the fact that there is no raised oestrogen level in castrated women without residual or recurrent malignant disease finds no explanation. It therefore seems reasonable to assume that tumour tissue itself is capable of oestrogen production. It is interesting that Dingemanse and collaborators in 1930 described the presence of large quantities of female sex hormone (menformon) in the blood of *male* and female cancer patients and that Silberstein and co-workers in 1932 found the same substance in the skin of a male patient with carcinoma of the rectum as well as in the tumour cells of human and mouse carcinoma.

Ayre and Bault (1946) have also drawn attention to the high endogenous oestrogenic activity noticeable in smears of uterine cancer patients but they believe that this is due to faulty nutrition causing liver impairment. However interesting this hypothesis is, it does not explain the selective persistence of high cornification levels in unsuccessfully treated cancer patients.

If the observation which we made in our 10 women of persisting high cornification indices in patients carrying malignant tissues can be corroborated in a larger material, the evaluation of the cornification index could provide a simple test of cure in follow-up examinations of uterine cancer patients. There is no accurate clinical or histological method of ascertaining that the treatment which a patient has received for malignant disease has been adequate and that no viable malignant cells have been left. Although our assumptions are based on a small number of investigations the preliminary results are promising and the subject seems important enough to encourage other investigators to test the reliability of our findings.

Summary

(1) Thirty-two of 38 post-menopausal women (84·2 per cent) suffering from cancer of the uterus had a high cornification index in their vaginal smears. This observation was independent of the histological type of carcinoma, whether squamous-celled or adenocarcinoma.

(2) Nine of 10 patients with recurrent or residual malignant disease of the uterus after radical treatment had a persistently high C.I., whereas 17 treated cancer patients without evidence of remaining disease had all cornification indices below 5.

(3) The significance and possible source of the raised cornification index are discussed.

(4) It is suggested that the cornification index be used as an indicator of cure or persistence of malignant growths of the uterus.

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RADIATION MENOPAUSE OR HYSTERECTOMY

Part II—Mortality, Reliability and Subsequent Pelvic Cancer

BY

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SEVERE uterine haemorrhage may be treated by hysterectomy or induction of an artificial menopause. The latter method is often used, especially in women over 40 years of age, because it is easier to perform and carries a lower immediate mortality than hysterectomy. It is said, however, that these immediate advantages of radiation may be offset by undesirable sequelae such as unusually severe menopausal symptoms or an added risk of cancer of the genital tract. The results published in Part I of this paper (Turnbull, 1955) suggest that one should not be deterred from inducing the menopause by radium because of the risk of causing severe or unpleasant menopausal symptoms; the incidence of such symptoms in a group so treated was practically the same as in a control group of women who had experienced a natural menopause. The present paper discusses these two methods of treatment from the point of view of primary operative mortality and morbidity, and the risk of subsequent cancer of the genital tract.

Corscaden, Fertig and Gusberg (1946) found 9 cases of endometrial and 6 cases of cervical cancer in a group of 958 women who had been treated with radium because of irregular bleeding at the menopause and followed up for an average time of 6·7 years. They calculated that by the age of 80, 9·6 per cent of women so treated would develop cancer in the uterine body. Speert and Peightal (1949) investigated a series of 270 cases with malignant disease of the uterine fundus and found that 21 (8 per cent) had previously been irradiated for benign conditions of the uterus. Since 6 of the 21 tumours contained sarcomatous tissue they concluded that radiation might predispose to the development of this type of malignancy. It is not clear from Corscaden's paper whether the chance of developing cancer of the fundus is increased by the use of radium or whether women with profuse and irregular uterine haemorrhage at the menopause have a greater risk of developing cancer than women who do not. One presumes that, had the 958 women been treated by hysterectomy, none would have developed cancer, but, assuming an operative mortality of 0·5 to 1 per cent, between 5 and 10 women would have died as a result of the operation while, at the time the paper was published, only 6 of the 15 cases who subsequently developed cancer had died of it and one had developed a recurrence. In the long run, the mortality might be very similar in both methods of treatment.

In view of the fact that in Aberdeen radium is used frequently to induce the menopause and because in a small compact region follow up of cases is relatively easy, it was thought that this problem of relative risks should be investigated. Almost all cases of female pelvic cancer in the Aberdeen area are treated in the Gynaecological Department and most of the cases occurring in private practice receive at least some of their treatment in hospital. Cases of cancer of the uterine body and cervix and of the vagina have been studied but not malignant tumours of ovary, urethra or vulva. The incidence of ovarian carcinoma following radiation for benign conditions is very low. Corscaden, Fertig and Gusberg (1946) found only 2 in 958 cases, followed up for an average of 6·7 years, while Hunter, Ludwick, Motley and Oaks (1954) found only 1 in 644 cases followed up from 2 to 20 years.

The first group studied consisted of 1,105

cases admitted to Aberdeen Royal Infirmary between January, 1938 and December, 1947, because of benign uterine haemorrhage and treated either by radiation to induce the menopause or by hysterectomy. Women under 30 years of age, and those who were treated for bleeding after the menopause, were excluded. Radiation was used in 739 (radium in 651 and X-rays in 88) and hysterectomy in 366 (subtotal in 94 and total in 272). Only 10 per cent of the cases treated by radiation were under 40 years of age compared to 35 and 45 per cent treated by subtotal and total hysterectomy respectively. Fibroids (including fibroid polypi) were present in 18 per cent of the irradiated cases, 78 per cent of the cases treated by subtotal hysterectomy and 57 per cent of those treated by total hysterectomy. Total hysterectomy was generally used where the cervix was lacerated or infected, whether fibroids were present or not, while subtotal hysterectomy was usually performed only when the cervix was healthy and least liable to malignancy—for example, in nulliparous patients with fibroids. This is illustrated by the fact that 56 per cent in the subtotal hysterectomy group and 10 per cent in the total hysterectomy group were nulliparous. No difference in parity distribution existed between the irradiated cases and those treated by total hysterectomy.

Immediate Mortality and Morbidity After Radiation and Hysterectomy

(a) *Mortality*

The mortality was 0·4 per cent in the irradiated cases and 0·8 per cent in those treated by hysterectomy. The 3 deaths after radiation were due to sepsis and occurred in 1942, 1943 and 1945 respectively. The histories were strikingly similar. In the first, bimanual examination before the radium was inserted suggested endometriosis. Pyrexia and diarrhoea developed 10 days later and the patient died 20 days later from generalized peritonitis, having been treated by the family doctor as a case of gastro-enteritis. The second case was admitted to a surgical ward 3 weeks after radiation because of generalized peritonitis. Laparotomy was performed and a left-sided pyosalpinx removed. A faecal fistula developed and the patient died during an operation to close it. The third case was readmitted to hospital with peritonitis 10 days after radiation and was treated conservatively. She died 10 days later and autopsy showed a left pyosalpinx with generalized peritonitis.

Two of the 3 deaths after hysterectomy occurred in 1943 and the third in 1945. One was due to pulmonary embolism 4 days after a total hysterectomy for large fibroids. The second was due to ileus and peritonitis 3 days after a total hysterectomy. The third resulted from intestinal obstruction 9 days after total hysterectomy for fibroids. A loop of ileum had become adherent in the pelvis. The patient died 12 hours after an operation to relieve the obstruction.

The mortality has also been studied in a more recent series of 802 cases of irregular uterine haemorrhage treated by radiation or hysterectomy between 1951 and 1953 in the Gynaecological Wards of both Aberdeen Royal Infirmary and Woodend General Hospital. Radiation was used in 497 and there were no deaths; hysterectomy in 305, with 1 death, a mortality rate of 0·32 per cent. The death was due to paralytic ileus and intestinal obstruction following total hysterectomy. The patient died after an operation to relieve the obstruction. Further details about this series are given in Table V.

Schmitze and Towne (1947) reported a mortality of 1·2 per cent in cases where the menopause had been induced by radium, but the deaths were due to intercurrent disease and not to the effects of radiation. Thornton, Nokes and Brown (1951) found 1 death in 348 cases (0·28 per cent). Hunter *et al.* (1954) found no deaths in 644 cases.

Hunter and co-workers (1954) report a death rate from hysterectomy of 0·5 per cent and, although very low rates have been published by American authors, the mortality rates from hysterectomy published in this country vary from 0·5 to 1 per cent. Table I shows some of the recent figures which are discussed later.

(b) *Morbidity*

In the 1938–1947 series, the incidence of immediate complications after hysterectomy (43·4 per cent) was 12 times greater than that after radiation (3·5 per cent). This difference was

TABLE I
Mortality Rates for Hysterectomy

Author	No. of Cases	Deaths	Mortality (per cent)
Doyle (1953)	6,248	Not stated	0·04
Burch and Lavelly (1952) ..	1,221	0	0
Cron, Stauffer and Paegel (1952)	1,000	2	0·2
Tyrone (1951)	2,000	4	0·2
Weaver and Johnson (1951)	884	1	0·1
Bell (1950)	3,602	52	1·4
	2,206 (fibroids only)	23	1·0
Burke (1950)	585	3	0·5
Green-Armytage (1950) ..	981	8	0·8
Gwillim (1950)	1,304	7	0·5
Hawkesworth (1950) ..	2,058	16	0·8
Kimbell and Rees (1950) ..	1,361	9	0·7
Mackenzie (1950)	1,051	17	1·6
Allen (1949)	640	1	0·16
Donnelly and Bauld (1949)	2,183	15	0·69
Siddall and Mack (1947) ..	2,451	19	0·78

due mainly to the absence after radiation of post-operative shock, chest and wound sepsis, paralytic ileus and intestinal obstruction. There was also a much lower incidence of infections in the urinary tract (0·8 per cent as against 9·3 per cent following hysterectomy). Since most of the radiation cases returned home within a few days of treatment, however, 0·8 per cent may be an underestimate. After hysterectomy, the incidence of post-operative shock requiring blood transfusion was 5 per cent, chest complications of various types 6·3 per cent, and wound sepsis 9·2 per cent, with complete disruption of the wound requiring re-suture in 1·9 per cent.

While the incidence of pelvic infection after radiation (1 per cent) was less than half that after hysterectomy (2·4 per cent) the severity of the complication was much greater for, as described above, 3 of the 7 cases died and another, mentioned later, required laparotomy; there were no deaths from pelvic sepsis after hysterectomy. During radiation, 10 cases (1·4 per cent) developed a "reaction" (pyrexia, abdominal pain or vomiting), but this subsided when the radium was removed and was not followed by pelvic sepsis. In 5, because of the severity of the symptoms, the radium had to be removed before the treatment had been completed, but in each case the amount of radiation given was sufficient to induce a permanent menopause.

After hysterectomy, 13 patients developed paralytic ileus or intestinal obstruction and 2 died. These complications did not occur at all in the cases treated by radiation.

The incidence of thrombo-embolic complications in the cases treated by radiation and by operation was 0·13 per cent and 1·64 per cent respectively. There was no case of pulmonary embolism after radiation, but 3 (0·82 per cent) occurred after hysterectomy with death in 1 case.

Acute mental disturbances occurred in 1 case after radiation (0·13 per cent) and in 4 after hysterectomy (1·1 per cent). Other complications occurred in 0·13 per cent of cases after radiation (proctitis, 1) and in 5 per cent of cases after hysterectomy (unexplained pyrexia 12; diarrhoea 3; severe vaginal bleeding 2; prolonged retention of urine 1).

Even where convalescence following hysterectomy is uncomplicated, the length of stay in hospital is 3 times that of the radiation cases and after discharge from hospital the patient takes longer to get to the stage when she can resume normal duties.

Although numbers in the present series are too small to allow of a completely reliable estimate of the relative mortality or morbidity of the two methods, it does seem that the mortality as a result of radiation is less than that from hysterectomy and the incidence of post-operative complications is very much less. It must be remembered, also, that radiation was used more often in older women and in those likely to be poor operative risks because of debility and anaemia, heart disease, hypertension or obesity. It is probable, therefore, that if such women had been treated by hysterectomy the operative mortality and morbidity in this series would have been higher.

LATE MORBIDITY AFTER RADIATION AND HYSTERECTOMY

Total hysterectomy cannot fail to cure uterine bleeding due to benign conditions, but this effect does not always occur after radiation.

On the other hand, late complications may follow hysterectomy which could not occur after radiation.

Of the 739 cases treated by radiation between 1938 and 1947, 33 or 4·5 per cent are known to have been re-admitted to hospital up to the end of 1953 with further symptoms unrelated to malignant disease. In 24 cases (3·2 per cent) this was because of recurrence of bleeding subsequently treated successfully by hysterectomy in 9 cases, by further radiation in 9 and by curettage alone in 6. In one half of the cases no cause could be found for the return of bleeding, in one quarter it was due to fibroids, and in the remaining quarter to cystic glandular hyperplasia of the endometrium. Of the 24 cases, 7 were under and 17 over 40 years of age at the time of the radiation—a recurrence rate of 9·3 per cent in the younger women and 2·5 per cent in those over 40 years of age at the time of treatment.

Of the remaining 9 cases, 6 were re-admitted because of vaginal discharge (erosion 3, pyometra 2, radium burn of the cervix 1). One had unexplained right-sided pain, one proctitis due to radium and one salpingitis due to radium. All 9 made a good recovery.

Of the 366 cases treated by hysterectomy 6 (1·6 per cent) are known to have been re-admitted to hospital. Only 2 of these had been treated by total hysterectomy. One had a vesico-vaginal fistula and the other intestinal obstruction; both were successfully operated on. The other 4 cases had been treated by subtotal hysterectomy. Two had cervicitis, one an incisional hernia and one a ureteral stricture. All were relieved of their symptoms by treatment although nephrectomy was necessary in the last case mentioned.

This analysis shows that the excess re-admission rate in the radiation cases was due to recurrence of uterine haemorrhage.

Subsequent Development of Cancer in the Uterine Body, Cervix or Vagina

Table II gives the incidence of cancer following radiation in some of the follow up studies published in the last 12 years. It is difficult to draw conclusions from them since the duration of the follow up varies greatly and because many cases of post-menopausal bleeding treated by radium have been included but not always differentiated.

Table III gives the Aberdeen findings. It shows that 10 (1·34 per cent) of the 739 radiation cases are known to have developed carcinoma of the uterus (6 cervix and 4 body of uterus) up to the end of 1953, i.e., over a period of 6 to 16 years. Of the 366 cases treated by hysterectomy, 3 (0·82 per cent) have developed cancer (1 cervix and 2 vaginal vault). The case of carcinoma of the cervix followed subtotal hysterectomy and the 2 cases of squamous carcinoma of the vaginal vault followed total hysterectomy.

The 4 cases who developed endometrial cancer were all multiparae. At the time the menopause was induced, 2 were 49 years of age and had normal endometrium while the other 2 were 51 and 55 years of age respectively and had cystic glandular hyperplasia of the endo-

Table II

The Incidence of Pelvic Cancer Following Radiation Menopause

Author	Number of Cases Irradiated	Number and Site of Subsequent Pelvic Cancers				Duration of Follow-up
		Corpus	Cervix	Ovary	Total	
Costolow (1941)	986	3	1	2	6	2½–12½ years.
Corscaden *et al.* (1946) ..	958	9	6	2	17	3 months–25 years. Average: 6·7 years.
Smith and Bowden (1948) ..	752	7	–	–	7	10 years or more.
Thornton *et al.* (1951) ..	348	6 (including 3 sarcoma)	1	1	8	6–21 years.
Montgomery *et al.* (1952) ..	851	9	2	1	12	6 months–21 years.
Hunter *et al.* (1954) ..	644	2	–	1	3	2–20 years.

TABLE III

The Incidence up to the End of 1953 of Subsequent Carcinoma of Uterine Body, Cervix and Vagina in 1,105 Cases of Benign Uterine Haemorrhage Treated by Radiation Menopause or Hysterectomy Between 1938 and 1947
(Percentages in brackets)

Treatment	No. of Cases	Carcinoma of Uterine Body	Carcinoma of Cervix	Carcinoma of Vagina	Total
Radium	651	4	4	–	8
X-ray	88	–	2	–	2
Total	739	4 (0·54)	6 (0·81)	–	10 (1·35)
Subtotal hysterectomy ..	94	–	1 (1·06)	–	1
Total hysterectomy	272	–	–	2 (0·74)	2
Total	366	–	1 (0·27)	2 (0·55)	3 (0·82)

metrium. Cancer was discovered respectively 13, 9, 5 and 12 years after the menopause was induced, and proved fatal in 3 patients; one woman is in good health 3 years after the diagnosis of cancer was confirmed.

Way (1954) found unsuspected endometrial carcinoma in 3 of 12 uteri removed from patients previously known to have had both a late menopause and endometrial hyperplasia, and has urged that such cases should be treated by hysterectomy. The fact that only 74 or 10 per cent of women in the radiation series were both over 50 and had cystic glandular hyperplasia of the endometrium and yet contributed 2 of the 4 cases of endometrial carcinoma supports this view.

Of the remaining 655 not believed to be specially susceptible to cancer of the body of the uterus, it did develop in 2 while 6 developed cancer of the cervix, a "body/cervix" ratio of 1 to 3.

In Aberdeen the relative frequency of cancer of the body and cervix after the menopause in women admitted to the Gynaecological Department is 1 to 3. This is the same relative frequency of body to cervix cancer as occurs in women treated by radium for benign bleeding and suggests that although the small amount of radiation given does not prevent the development of endometrial cancer it does not predispose to it.

The 6 cases where cervical cancer developed after radiation (Table III) were multiparae. At the time when the menopause was induced, their ages ranged from 42 to 52 years and cancer was diagnosed 10, 9, 8, 4, 3 and 1¼ years later. Three have died of the cancer and 3 are alive without evidence of recurrence 2, 3 and 5 years after the diagnosis was made. The cervix was noted to be hypertrophied, lacerated and eroded in 5 of the 6 cases when the menopause was induced, and it is possible that biopsy might have revealed carcinoma *in situ*.

The cancer of the cervical stump was found 8 years after subtotal hysterectomy for large uterine fibroids in a woman of 40 who had had one pregnancy. The fact that the cervix was judged to be "healthy" at that time is a reminder that, when hysterectomy is performed, the cervix should be removed whenever possible, especially in parous women. Fortunately, this patient was alive and well 7 years after the cancer was discovered.

The 2 cases where squamous carcinoma developed in the vaginal vault after total hysterectomy had each had 1 pregnancy, and were 33 and 48 years of age respectively when the operation was performed. Uterine fibroids were present in both; in 1 the cervix was noted to be lacerated, and in the other a small mucous polyp was found in the cervical canal. Vault cancer was found 7 and 6 years later. One patient has died of cancer while the other is still alive and without recurrence 8 years after the cancer was diagnosed.

In view of the great rarity of primary squamous carcinoma of the vagina, especially at the vaginal vault, it seems probable that in the 2 cases in this series it developed from remnants of cervix left at the time of operation.

The time interval, 6 and 7 years respectively, makes it unlikely that overt carcinoma was present in the cervix when hysterectomy was performed. Dunster and Bennett (1953) have described 3 cases of squamous carcinoma developing in the vaginal vault after total hysterectomy and have obtained information from other centres about several other cases.

In this series, the incidence of cancer of the vault after total hysterectomy (2 out of 272 or 0·74 per cent) is similar to that of cancer of the cervix after radiation (6 out of 739 or 0·81 per cent). It must be remembered, of course, that total hysterectomy was selected as the method of choice where the cervix looked "unhealthy". Finn (1952), for example, found unsuspected cervical cancer (Stage O or I) in 1·12 per cent of 1,876 uteri removed for apparently benign lesions, while Auerbach and Pund (1946) found that 3·9 per cent of 1,200 uteri removed by total hysterectomy showed pre-invasive cervical carcinoma. It is not stated in either of these papers whether or not any of the patients with carcinoma *in situ* had a recurrence in the vaginal vault.

The Incidence of Previous Radiation or Hysterectomy in Cases of Cancer of the Uterus and Vagina

Taylor and Beckner (1947) found a history of previous radiation for benign lesions in 4·97 per cent of 531 cases of carcinoma of the uterine body, and Smith and Bowden (1948) 1 per cent of 805 cases. Speert and Peightal (1949) found a very high incidence (8 per cent) in 270 cases, but of the 21 cases developing malignant disease (including 6 with sarcomatous elements), 1, diagnosed 8 months after radiation, was probably present at the time of the original treatment; 6 had apparently had radiation because of bleeding after the menopause; 1 had a caruncle irradiated; and in another case a temporary menopause was induced in a woman of 21 years of age. If these cases are excluded, the percentage becomes 4·4, very similar to that found by Taylor and Beckner.

These papers did not indicate whether the percentage of cases with a history of induction of the menopause was greater in cancer of the body of the uterus than in other types of pelvic cancer.

A search was therefore made for a history of induction of the menopause or hysterectomy in the records of 860 cases of primary cancer of the uterine body, cervix or vagina, admitted to the Aberdeen Royal Infirmary during the period 1938–1953.

Table IV shows that out of 124 cases of carcinoma of the body of the uterus, 4 and possibly 5 (4·0 per cent) and 7 of 683 cases of carcinoma of the cervix (1·02 per cent) had previously had the menopause induced by radiation. Ten of these cases (4 endometrial and 6 cervical cancers) have been described in the previous section. The fifth case of endometrial cancer developing after radiation was a nullipara aged 54 years who stated that 5 years previously she had been admitted to the Aberdeen Royal Infirmary and treated by X-rays

Table IV

Incidence of Previous Radiation Menopause or Hysterectomy in 860 Cases of Cancer of Uterine Body, Cervix or Vagina
(Percentages in brackets)

Type of Carcinoma	Total Cases	Previous Treatment		
		Radium or X-ray Menopause	Subtotal Hysterectomy	Total Hysterectomy
Carcinoma of Body	124	5* (4·0)	–	–
Carcinoma of Cervix	683	7 (1·0)	6 (0·9)	–
"High Endocervix–Low Body" Carcinoma ..	15	–	–	–
Sarcoma of Uterus	15	–	–	–
Carcinoma of Vagina (Squamous only) ..	23	–	–	5 (21·7)

* Including 1 case where the history of previous radiation treatment could not be confirmed.

to induce the menopause. No record of this admission could be traced. The seventh case of cervical cancer occurring after radiation was 55 years of age and had had 9 pregnancies. Nineteen years before, curettage had been performed and a large erosion cauterized. Seventeen years before, the menopause had been induced by radium in a dosage of 3,600 mg. hours. At that time, the cervix was described as "atrophied and fissured" but no biopsy was taken.

Although a history of induction of the menopause by radium was obtained in 4 or possibly 5 cases of carcinoma of the body of the uterus, 2 of the patients were over 50 and had endometrial hyperplasia when irradiated; it has already been shown in the previous section that such cases may have a special predisposition to develop endometrial carcinoma. Nevertheless, even if these 2 women had been treated by hysterectomy instead of radium, a history of irradiation menopause would still have been twice as common in cases of endometrial cancer as in cases of cervical cancer. But, of course, a considerable proportion of the women with cervical cancer, unlike those with endometrial cancer, were too young to have required induction of the menopause. Thus, in comparing cases of cervical and endometrial cancer in respect of a history of induction of the menopause, only those where the cancer developed after the menopause can be used. About half the cases of cervical cancer occur in post-menopausal women, so that the percentage with a history of menopausal radiation is almost double that for all age groups; but since almost all cases of endometrial cancer occur after the menopause, the percentage in post-menopausal women is about the same as that for the whole group. Thus, in comparable groups of the two types of cancer, the percentage in which the menopause was induced is very similar.

It seems, therefore, that women who have irregular bleeding at the time of the menopause, whether treated by radium or not, are no more liable than average to develop cancer of the body of the uterus, except for those over 50 years of age with irregular bleeding associated with glandular hyperplasia of the endometrium.

Of the 6 cases where cancer developed in the stump left after subtotal hysterectomy, 1 has already been described in the previous section. The other 5 cases were diagnosed 7, 17, 18, 19 and 20 years respectively after operation. All the patients were multiparae, and the operation was performed for fibroids in 3, for chronic pelvic pain in 1 and for severe concealed accidental haemorrhage in 1.

The fact that 6 (0·9 per cent) of 683 cases of cervical cancer occurred in the stump left after subtotal hysterectomy and that all 6 women had had at least one child suggests that even if the cervix looks "healthy", total hysterectomy rather than subtotal should be performed. Yet of 23 women with squamous carcinoma of the vagina, 5 (21·7 per cent) had previously undergone total hysterectomy and in all 5 the tumour was in the vault. Of these 5 cases, 2 have already been described. Each of the other 3 was parous. In the first, operation was performed in a woman of 59 years because of pyometra, but no histological evidence of malignancy was found in the cervix, fundus or ovaries at that time. In the second, uterine fibroids were present; the cervix was not examined histologically. In the third, bilateral ovarian serous cystadenomata were found in a woman of 65 years but there was no histological evidence of malignancy in the cervix, fundus or cysts. Squamous vault cancer was diagnosed 5, 10 and 3 years later, respectively. It is unlikely that overt carcinoma was present in the body of the uterus or the cervix at the time of operation because of the time intervals. These findings are similar to those of Dunster and Bennett (1953) who reported that in 11 cases of carcinoma of the vagina, 3 (of squamous type) were situated in the vaginal vault and, in each of these, total hysterectomy had been performed previously for a benign condition. In their cases, the intervals between the operation and the diagnosis of cancer were 6, 8 and 12 years respectively. If, as they suggest, the tumour develops from carcinoma *in situ* in a remnant of cervical tissue left at the time of operation, removal of a cuff of vagina wherever possible might lessen the risk of cancer. In some cases this might be dangerous, especially where there is deep laceration of the cervix and much fibrosis.

Discussion

What is the relative place of radiation and hysterectomy in the treatment of irregular uterine haemorrhage in cases where conservative methods have failed? Table V shows that in Aberdeen between 1938 and 1947 radiation was used in over 90 per cent of women over the age of 40 where no fibroids were present. In women under 40 it was still used in 60 per cent of cases. Where fibroids were present hysterectomy was the method of choice, especially in women under 40 years of age (85 per cent). By the years 1951–1953 greater use was being made of hysterectomy for fibroids and functional bleeding, but even then, in the absence of fibroids, radiation was still used in 88 per cent of women between the ages of 40 and 49.

With regard to the relative safety of the two methods, the immediate mortality for hysterectomy in the original series is twice that for radiation, 0·82 and 0·41 per cent respectively. In the more recent series the death rate from hysterectomy was only 0·32 per cent (1 death in 305 cases), but there were no deaths in 497 cases treated by radiation. It seems, therefore, that the immediate risk of death is greater if hysterectomy is used. It is difficult to say how many more women would have died if hysterectomy had been the only treatment available. Many patients treated by radiation were in such poor health as to be poor operative risks.

With regard to the effectiveness of the two methods, it is true that radiation is not effective in stopping the bleeding in all cases, as is the case with hysterectomy; but the incidence of recurrence of bleeding was low, 3·2 per cent, and was effectively dealt with on the second occasion. Radiation has the advantage that the patient's stay in hospital after treatment is only one-third of the time required for uncomplicated convalescence after hysterectomy and there is very little post-operative morbidity—only one-twelfth of that following hysterectomy. Also the late sequelae in the radium group, although more common, consist mostly of return of bleeding which is not as a rule serious. In the operation group late complications, although infrequent, are more serious, vesico-vaginal fistulae, incisional hernia, or ureteral stricture necessitating nephrectomy.

Since most of the women treated by radiation were in the middle forties the induction of the menopause was not a great hardship, particularly as many had flushings and other menopausal symptoms before treatment was given. There was no indication that menopausal symptoms were more severe, following radiation, than in the normal menopause. The greatest drawback to radiation is the development of cancer of the cervix or body of the uterus subsequently.

There is no evidence that radiation increases the chance that cancer will develop in the pelvis, but it cannot, unlike hysterectomy, reduce the

Table V

Distribution by Type of Treatment of Benign Uterine Haemorrhage in 1,105 Cases Treated Between 1938 and 1947, and in 802 Cases Treated Between 1951 and 1953

Group	Age	Total	Fibroids			Total	Others		
			Radiation	Hysterectomy	Percentage Hysterectomy		Radiation	Hysterectomy	Percentage Hysterectomy
1938	30–39	67	10	57	85	162	65	97	60
to	40–49	231	92	139	60	484	455	29	6
1947	50+	65	32	33	50	96	85	11	11
	Total	363	134	229	63	742	605	137	18
1951	30–39	39	1	38	97	124	22	102	82
to	40–49	125	30	95	76	408	360	48	12
1953	50+	29	14	15	52	77	70	7	9
	Total	193	45	148	77	609	452	157	26

chance. If the number of deaths which have subsequently occurred from cancer be added on to the primary mortality in the appropriate group, the total mortality (early and late) is about the same in both groups since the lower primary mortality in the radiation series is compensated for by the smaller number of deaths from cancer in the operation group. It has to be remembered that more of those women treated by radiation between 1938 and 1947 may still develop cancer but, of course, the fact that they have had many years of life before the cancer develops is to be put to the credit of radiation treatment whereas the operative death is sudden and unexpected and occurs in fairly young women at what may be a critical point in the family life. The fact that 2 cases of cancer of the vaginal vault developed out of 272 cases where total hysterectomy had been performed is a reminder that this operation does not guarantee that cancer will not occur in the pelvis. Of the 6 cases where cervical cancer developed after radiation, one was found within a year and almost certainly was present at the time of the radiation. In the others there was an interval of up to 10 years, suggesting that carcinoma *in situ* may have been present at the time of the original treatment. If extensive "ring" or "core" cervical biopsies were taken in all cases where radiation was to be used, whatever the appearance of the cervix, the chance of finding unsuspected *in situ* or Stage I cancer would be considerably increased. Routine examination of cervical and vaginal smears might also help in diagnosing these early cancers, which were probably present in at least 0·8 per cent of the cases in the series treated by radiation between 1938 and 1947.

The conclusions which we have drawn from the findings in this paper are that, at present, the best results, both short and long term, are likely to be obtained by a judicious use of both methods. If a very low mortality rate could be achieved where *all* cases were treated by hysterectomy, there would be something to be said for giving up the use of radium and X-rays. Otherwise, the question is—what proportion should be treated by radiation?

This might depend on such local considerations as the availability of experienced gynaecologists and nurses, the length of waiting lists and the level of health and physique of the patients. As a working plan, however, hysterectomy could be performed in all reasonably fit women under 40 years of age, and in those over 50 years of age where the endometrium showed cystic glandular hyperplasia. In the younger women, postponement of menopausal symptoms would be achieved with comparatively little risk and, in the older women with metropathia, the probable increased tendency to cancer of the body of the uterus would justify the risk of operation. There is still a good deal to be said for radium or X-rays in women over 40 years of age, particularly when the risks of operation are increased by factors such as adiposity, hypertension or debility. In all cases where radiation is to be used, vaginal and cervical smears and an adequate biopsy of the cervix should be examined to minimize the risk of overlooking cancer *in situ*. By this policy, the number of deaths following hysterectomy would be kept low and the risk of death from cancer in those treated by radiation would be reduced to a minimum.

The extent to which hysterectomy should be used may turn on the mortality of the operation. Morbidity must also be taken into account in deciding about the best method of treatment. Unfortunately, most publications on mortality after hysterectomy do not indicate clearly the extent to which other forms of treatment are used for "poor-risk" cases. Some of the series quoted in Table I which show very low mortality rates, being private cases, are not representative of a total community. Women in the upper social classes are usually of better physique and seek medical advice sooner than those in the lower social classes. It is likely that they will stand operation better and have a lower death rate.

Therefore the relative merits of the two methods of treatment of benign uterine haemorrhage can only be assessed accurately by a study of mortality and morbidity in a very large series in which *all* cases treated are studied. It would be most valuable to know the results of treatment for this condition in other units, particularly in those where radiation is not used.

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ACUTE FATTY LIVER OF PREGNANCY

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IN a long article on the pathology of acute yellow atrophy and delayed chloroform poisoning in the pregnant woman, Sheehan (1940) divided cases of clinical acute yellow atrophy into three main categories: true acute yellow atrophy, obstetric acute yellow atrophy, and delayed chloroform poisoning.

The pathology of obstetric acute yellow atrophy is regarded as fundamentally different from that of any type of hepatic necrosis and is almost certainly a distinct entity in which the liver change is solely that of fatty accumulation. Although the pathology of true acute yellow atrophy and of chloroform poisoning is now well accepted, the condition of obstetric acute yellow atrophy has been almost completely ignored; recent surveys on liver disease by Himsworth (1950), the Ciba Symposium (Sherlock, 1951), and Javert and Morrison (1951) do not discuss it at all, and Browne (1951) and Dieckmann (1952) give a summary of Sheehan's article, but add no further information. Some explanation for this neglect may lie in the rarity of the disease. Lock, Burt and Lide (1953) mentioned obstetric acute yellow atrophy but did not find an example among their 21 fatal cases in pregnancy in which liver failure was either a primary cause of, or was contributory to death. Ingerslev and Teilum (1951), in their study of 91 cases of jaundice occurring in pregnancy, made no reference to obstetric acute yellow atrophy; they conclude that all or almost all of their cases were infective hepatitis, and the one maternal death recorded by them was a true acute yellow atrophy.

The present paper deals with the findings in 4 cases of acute liver failure in pregnancy. Of these 2 died and 2 recovered. The clinical picture and pathology are closely in accord with those cases described by Sheehan. (The tissues of one further fatal case have been studied; both clinically and pathologically it is similar to the fatal cases recorded in the present paper.)

CASE NOTES

Case 1, M.A.F., 12036, age 36 years, para-2, was admitted at 30-weeks gestation when she complained that 10 days previously her appetite became poor, that she felt depressed and that for the previous 2 days she had been vomiting. Her own doctor had examined her 5 days before admission and found that her blood pressure was 140/90 and that there was a slight albuminuria. When admitted she was jaundiced and was vomiting "coffee grounds" material. She was confused mentally. Albumen and bile pigment were present in the urine and her blood pressure was 150/90. There was no pyrexia. Treatment consisted of intravenous glucose, aureomycin and penicillin. On the day following admission she became "insane" and mildly violent. At this time the blood urea was 100 mg. per 100 ml. and the serum bilirubin was 9·3 mg. per 100 ml. Investigations for leptospirosis gave negative results. She had a spontaneous delivery of a deadborn foetus later that day. Haematemesis occurred during delivery. Following the delivery she became shocked, had convulsions and passed into coma. In spite of blood transfusion she died on the 2nd day after admission, some 5 days following the onset of vomiting, and 13 days after the onset of her illness.

The relevant autopsy findings were as follows: There was a purplish ecchymotic rash over the anterior abdominal wall, chest, hips and thighs. Herpetic lesions were present on the lips. The brain showed no lesions of Wernicke's encephalopathy. Both pleural cavities and the abdominal cavity contained bloody effusions. There was some retroperitoneal haemorrhage. The stomach contained "coffee grounds" material but no bleeding point was demonstrated anywhere in the intestinal tract. The liver weighed 1,380 g.; it was of a uniform yellow colour. The gall bladder and extra-hepatic biliary system were quite normal and the hepatic veins contained no thrombus.

Case 2, C.R., 16252, age 34, para-6, attended the antenatal clinic when she was about 23-weeks pregnant. At this time she was in quite normal health and her haemoglobin was 11·8 g./100 ml. When she was 27-weeks

pregnant she had a short attack of vomiting which lasted a few days and she also had nose bleeds. At 30-weeks gestation her vomiting recurred and proved intractable. A week later she developed jaundice and was admitted to hospital. Laboratory studies gave the following results. The urine contained bile, acetone, pus and *Bacterium coli*. The serum bilirubin was 6·0 mg., the blood urea 63 mg., the serum potassium 13 mg., and the serum sodium 325 mg. per 100 ml. Intravenous glucose was given but 24 hours after admission her condition had deteriorated; the jaundice was more intense and she had "coffee grounds" vomiting. Clinical chemistry: serum bilirubin 7·3 mg., blood urea 56 mg., serum potassium 13 mg. and serum sodium 320 mg./100 ml. A Caesarean section was carried out and a small portion of liver was removed at the same time for histology. The gall bladder was palpated and there was no evidence of cholelithiasis. Following the section 1 litre of 5 per cent dextrose containing 1 per cent choline chloride was given over 24 hours. Twelve hours after the beginning of the intravenous therapy her serum values were: bilirubin 6·3 mg., urea 111 mg., potassium 13 mg. and sodium 375 mg. per 100 ml. "Coffee grounds" vomiting persisted for about 1 day following the commencement of intravenous therapy. In view of the low serum potassium, 300 ml. of Darrow's solution was given intravenously. Thirty-six hours following the commencement of therapy her serum values were: urea 122 mg., potassium 14·5 mg., and sodium 325 mg. per 100 ml., and at 60 hours the serum values were: bilirubin 3·5 mg., urea 106 mg., potassium 14·5 mg., and sodium 345 mg./100 ml.

She rapidly improved and was discharged on the 15th day following admission.

There had been no rise of temperature at any time. Investigations for leptospirosis had proved negative.

Case 3, M.D., 19757, age 28, para-1, attended the antenatal clinic when she was at 37-weeks gestation; no abnormality was found. She was admitted in labour 5 days later and had a normal delivery of a deadborn foetus weighing 5 pounds 13 ounces some 8½ hours after admission. Forty minims of chloroform followed by ether were administered during labour. At the time of delivery no clinical cause for the death of the foetus was found, and the patient was apparently normal. Nineteen hours after delivery (27 hours following admission) jaundice was first noticed. This was accompanied by a burning pain in the epigastrium and there was some abdominal distension. At this time laboratory investigations disclosed: haemoglobin 11·8 g., haematocrit 40 per cent; urine, albuminuria; serum-bilirubin 11·0 mg., and urea 72 mg. per 100 ml. Fifty-five hours after delivery her mental state was confused and she had hiccough; there was free fluid in the abdomen. At this time laboratory investigations showed: thymol turbidity and flocculation nil, serum alkaline phosphatase 54 King-Armstrong units, bilirubin 12·6 mg., and urea 120 mg. per 100 ml.; the faeces contained bile and the urine contained bile and urobilinogen. At about 70 hours after delivery she was deeply comatose. An intravenous drip of 5 per cent glucose containing 10 g. choline chloride per litre was set up and continued for 12 hours. This therapy was followed by the intravenous administration of a commercial dextrose—fibrin hydrolysate solution (Aminosol; Abbott); Glutamic acid and vitamin B complex were also given. Eighty hours after delivery laboratory investigations showed: urine ammonia 0·01 g. NH_3, the prothrombin index was 0·7 and this was unaltered 24 hours after the injection of 100 mg. vitamin K.

At about 20 hours following the start of intravenous therapy the patient began to improve and consciousness was recovered completely 43 hours after the start of treatment. Shortly after this time the serum bilirubin was 16·8 mg., and the blood urea 109 mg. per 100 ml. Thereafter she slowly improved, though her mental state was confused and she had attacks of delirium for a few days.

On the 13th day after delivery the prothrombin index was 1, the serum bilirubin was 2·5 mg., and the blood urea 35 mg. per 100 ml. A needle liver biopsy was performed on that day, and she was discharged 15 days after delivery. She had had a total of 7½ g. streptomycin and 21 mega units of penicillin during her stay. Her urinary output was satisfactory throughout. Investigations for leptospirosis were negative.

Case 4, O.B., age 22 years, para-2, was admitted at 36 weeks gestation because of vomiting, pains in the back, and sleeplessness. She had been well until 2 weeks before admission, since when she had complained of anorexia and vomiting. At the time of admission she was vomiting after all types of food, she had pain in the back, but her bowel function and micturition were normal. Clinical examination disclosed no abnormal signs. Clinical chemistry: blood urea 40 mg./100 ml.; urine contained traces of albumen and glucose, and her haemoglobin value was 9·6 g.

On the day following admission the patient developed intense epigastric and dorsal pain. She collapsed after vomiting 5 to 6 ounces of dark brown fluid. There was no shock. She improved with intravenous glucose and sedatives.

At about 72 hours after admission the patient became comatose following a period of restlessness and jaundice was noted. The treatment given was intravenous dextrose saline, methionine and vitamin B complex.

Laboratory investigations at about this time showed: a positive direct serum bilirubin with a total value of 4·4 mg./100 ml., a normal thymol turbidity and a serum alkaline phosphatase of 50 King-Armstrong units.

At about 84 hours after admission, the patient was delivered of stillborn twins; the first was macerated and the second was estimated to have been dead for 24 hours. Five minutes after the delivery of the placenta the patient collapsed and the blood pressure was not recordable. The patient regained consciousness following intravenous dextraven and blood but she continued to be drowsy and had difficulty in speaking.

At about 120 hours following admission her jaundice was deeper, she was less co-operative and less mentally alert. Laboratory investigations showed: a haemoglobin

value of 6·6 g., a total white cell count of 31,000 per c.mm.; a blood urea of 86 mg. per 100 ml., a uric acid value of 8 mg. per 100 ml., a serum potassium of 18 mg. and serum chlorides of 722 mg. per 100 ml. Tests of liver function were as follows: a serum bilirubin of 9·1 mg. per 100 ml., with a strong positive direct reaction, a normal thymol turbidity and a serum alkaline phosphatase value of 19 King-Armstrong units. (A further value of 10 was obtained later.)

At 144 hours she was more deeply jaundiced. Treatment with intravenous dextrose, dextrose saline and 1 per cent methionine was continued but she died some hours later, i.e., at about one week after admission.

The liver at autopsy was normal in shape and size and there was an obvious lobular pattern of dark red specks upon a pale greenish bronze background. No haemorrhages or evidence of necrosis were found. Other relevant autopsy findings were jaundice, gastric sub-mucosal haemorrhages, subendocardial haemorrhages in the left ventricle and a purulent bronchopneumonia. The extrahepatic biliary system was normal and the pancreas showed no abnormality either to the naked eye or histologically.

The following cases reported in the literature have, on the grounds of the histological picture of the liver, been accepted as examples of this disease: Stander and Cadden (1934); Cullinan (1936), Cases A and B; Sheehan (1940), 6 cases; Whitacre and Fang (1942); Nixon *et al.* (1947), Case 20, and Dill's Cases 2 and 6 (1950). Stander and Cadden, Cullinan, and Dill called the condition either acute or subacute necrosis, or acute yellow atrophy. The other authors recognized the liver pathology as one of fatty change.

There are, of course, many other reports of fatal and non-fatal cases of acute yellow atrophy in pregnancy, some of which have no information on the liver pathology while others are examples of necrosis of the liver. None of these reports are included in the present paper.

Clinical Comment

Sheehan summarized the clinical findings of his cases as follows: "at 36 to 40 weeks there was a sudden onset of severe vomiting and epigastric pain followed in a few days by jaundice. These symptoms progressed rapidly, the jaundice became very intense, the vomit was of coffee grounds appearance, and headache was sometimes present. After 7 to 12 days the patient was delivered of a stillborn foetus, became comatose and died within three days after delivery." The similarity of this clinical picture to that of true acute yellow atrophy was emphasized by the author. The acceptable cases in the literature fit into this clinical picture with but minor differences—in some, for example the whole course may occupy only 5 or more days. Cases 1 and 4 of the present series also had much the same course as described by Sheehan, but Case 3 differed in that the onset was heralded by jaundice after the delivery; Case 20 of Nixon *et al.* (1947) similarly commenced in the early puerperium.

The cerebral state is of importance since it is indicative of the severity of the liver failure. In Cases 1 and 3 the progress of the disease was accompanied by violent cerebral disturbances. Case 1 was mentally confused on the day of admission, became "insane and mildly violent" the next day and had convulsions immediately following the delivery. As has been noted, there was no suggestion of Wernicke's encephalopathy at autopsy. In Case 3 mental confusion was noted at 1½ days following the onset of the jaundice; deep coma followed 15 hours later. On the return of consciousness, however, the patient became violent and delirious. In the earlier cases of this condition reported in the literature cerebral disturbances have also been noted (Stander and Cadden, 1934; Cullinan, 1936).

The most important features of the clinical state are that it is a severe acute liver failure, that true acute yellow atrophy is simulated and that death frequently occurs.

Toxaemia of pregnancy was associated in 3 of the whole series of 17 cases which have been reported here and in the previous literature.

Pathology

The following description is based on the present fatal cases and on the acceptable fatal cases recorded in the literature.

The liver usually weighs less than normal; Sheehan (1940) for his 6 cases gives the range 1,040–1,300 g., and in 6 other cases the range is from 1,300 g. to 1,380 g. In none of these instances could the liver be regarded as atrophic. However in Case 20 of Nixon *et al.* (1947), which seems, from the histological description to be quite typical, the liver only weighed 860 g.

To the naked eye the liver is of a uniform pale colour and this appearance has been recorded by

most observers. Cullinan (1936) in his Case A found haemorrhages under the capsule and on section, and Dill (1950) also described subcapsular haemorrhages on the surface. The liver of Case 4, too, is rather different in that there was an obvious lobular pattern of dark red spots on a pale greenish bronze background.

No abnormality is seen at the porta, and the gall bladder and extra-hepatic biliary system are normal. The kidneys are normal, both to the naked eye and histologically, and contain no stainable fat. In most descriptions a prominent feature at autopsy is that of haemorrhage in various sites. In Case 1 of the present series there was bleeding into the skin, pleura, peritoneal cavity and the retroperitoneal soft tissues, and in Case 4 gastric submucosal haemorrhages were seen. In these cases, as in the others reported in the literature, there is little else of note, other than bile-staining of the tissues.

The following description of the histology of the liver is based on the above fatal cases, on the biopsy tissue from Cases 2 and 3 of the present series and on the biopsy of the recovery case of Whitacre and Fang (1942). The liver in Cases 1 and 4 was much more severely involved than in Cases 2 or 3.

The cardinal lesion affects very sharply the centrolobular area of every lobule. The liver cells surrounding the central vein are bloated and vacuolated and in almost all cases appear tightly packed together (Fig. 1). In one instance (Case 4), however, the liver sinusoids were prominent and the liver columns were well separated. In sections stained haematoxylin and eosin the cytoplasm of the affected liver-cell is broken up into innumerable fine vacuoles between which the cytoplasm is stretched in fine strands (Fig. 2). In frozen sections it is seen that the vacuolation is due entirely to fat which with Sudan stains gives the reactions of neutral fat (Fig. 3). It is distributed as a fine foam throughout the cell cytoplasm; the appearance has been likened to that of cells of the supra-renal cortex. Only rarely do the fine droplets fuse to produce the classical picture of a fatty cell, i.e., a cell distended by one or two large globules. No extracellular fat is present. There is no cholesterol nor iron either in the affected or in the unaffected liver cells.

The extent of the fatty change varies from case to case and from lobule to lobule but even in the most extensive there is always a narrow periportal rim of liver cells which are for the most part quite normal, though some of them may show a fine vacuolation. Large globules of fat were present in some periportal cells in the biopsy of Case 3 and in Case A recorded by Cullinan (1936).

The nuclei in the foamy cells are normal. In a few cells the nucleus may stain faintly and occasionally in others the nuclei may show some pyknosis, but the variability of nuclear staining differs little from that seen in any normal liver. The reticulin pattern of the liver is quite normal; there is no condensation nor increase in amount of reticulin or collagen at the portal tracts (Fig. 4).

In all four specimens of the present series the liver cells contain bile pigment, both in the fatty and in the normal cells. In addition bile thrombi are present in 2 out of 4 cases; these are found in the bile canaliculi between the fatty liver cells of the centro-lobular areas and to a much lesser extent between the normal cells of the periportal region. No bile thrombi can be found in the bile channels of the portal tracts.

In 3 of the 4 cases the Kupffer cells contain brown granules which are presumably bile pigment.

Cellular infiltration is not a prominent feature. A few polymorphonuclear leucocytes and mononuclear cells may be found in the portal tracts and occasionally infiltrating towards the centre of the lobule, but cellular aggregations are never gross.

In the present cases and those in the literature, the liver specimens, whether at biopsy or autopsy, were taken at between 5 and 16 days after the onset of the illness. There were marked differences in the extent of the fatty change but for each individual affected liver cell the appearances were the same, and, in particular, there was never any necrosis. In the single case recorded by Whitacre and Fang (1942) a biopsy was carried out at 6 days and also at 14 days following the onset of the illness. The 14-day biopsy showed a much less extensive fatty change, in that, although the centro-lobular cells were fatty, the periportal rim of unaffected

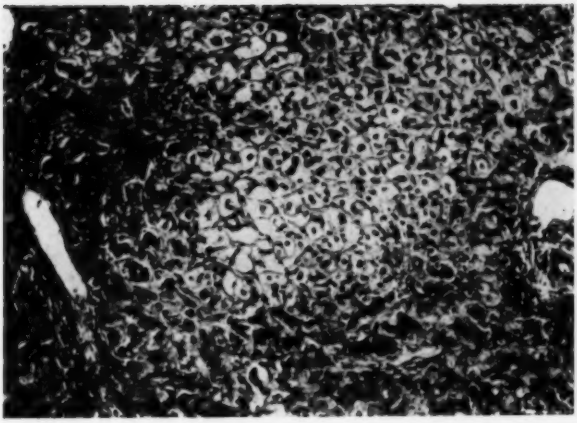

FIG. 1
Centro-lobular bloating and vacuolation of liver cells. Haematoxylin and Eosin. ×100.

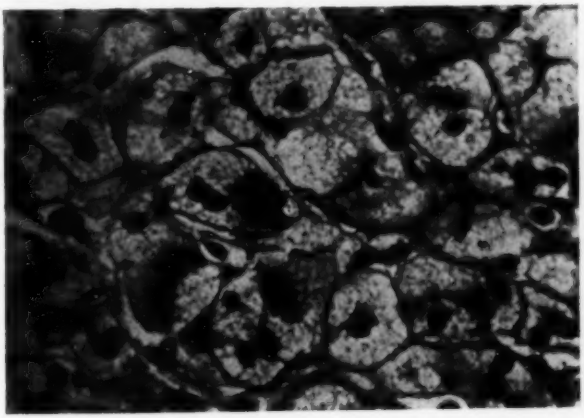

FIG. 2
Foamy appearance of affected liver cells. Haematoxylin and Eosin. ×450.

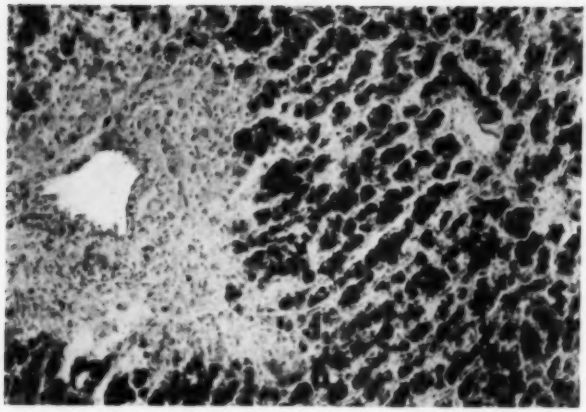

FIG. 3
Fatty character of cells of centro-lobular area. Sudan 3. ×100.

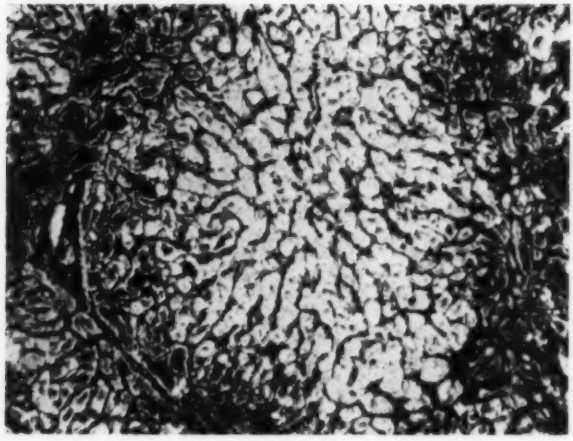

FIG. 4
Normal architecture of liver is retained. The affected centro-lobular area is well shown. Reticulin stain. ×100.

cells was thicker. There was no evidence at the centre of the lobule of progression towards necrosis, nor of healing of a previous necrosis.

It should be mentioned at this point that no examples of this disease have been found in non-pregnant females nor in males. The association of a fatty liver of this type with clinical acute liver failure would appear to occur only in the pregnant woman.

Discussion

The Nature of the Liver Lesion

From the present cases it is quite clear that the observable disturbance in the liver is one of fatty change mainly in the central parts of the liver lobule. Necrosis does not occur and the liver pattern remains normal.

In a survey of the literature cases have been quoted which, from the descriptions given and from the illustrations where available, are identical with the cases personally observed. It is apparent, however, that some authors, whilst accepting the fact that there is no necrosis in the tissue they examined, believe that the fatty change is an early stage of a true necrosis which would have become histologically recognizable had the patient lived longer (Stander and Cadden, 1934; Cullinan, 1936). Dill (1950), in an extensive survey of acute yellow atrophy in pregnancy, restricts his discussion to the details of the relationship between viral hepatitis and acute yellow atrophy, i.e., acute massive necrosis. He describes 6 fatal cases of which his Case 3 appears to be that recorded by Stander and Cadden (1934). His Cases 2 and 6 are identical with the fatal cases recorded here. He does not describe necrosis as a feature, but nevertheless he places these cases in the same group as acute massive hepatic necrosis. Whitacre and Fang (1942) are more definite. They state that they did not find necrosis but they assume that the fatty change described is but a stage in the development of necrosis due to viral hepatitis. They regard the pathological entities of acute hepatitis, toxic hepatitis and obstetric acute yellow atrophy as milder forms of acute yellow atrophy.

Sheehan (1940), describing his 6 cases which died at 10 to 15 days from the onset, maintained that at no time could necrosis be seen. In the present series liver tissue was examined at periods between 7 and 14 days following the onset, and in none of these was necrosis seen.

It is argued with Sheehan that, even with slowly acting toxins, necrosis of parenchymatous organs is manifest within a day or so. Certainly by this time a liver necrosis such as follows chloroform, carbon tetrachloride or phosphorus would be obvious. On the other hand, in obstetric acute yellow atrophy, necrosis is never observed although the clinical course may occupy 15 days. This is strong evidence that the fatty change is not the prelude to a necrosis.

The assumption that fatty change of the degree found in this syndrome is an early stage of the necrosis of acute infective hepatitis is certainly not borne out by the descriptions of the sequential liver changes in the latter disease (Hadfield, 1953). Furthermore Nixon *et al.* (1947) distinguish quite clearly between infective hepatitis of pregnancy and a condition they call pregnancy icterus. Their Cases 19, 20 and 21 fall into the latter group and, of these, Case 20 can be accepted as identical with the present cases. (There was no biopsy of Case 21 and in their Case 19 there were only slight changes in the liver, the histological evidence of fat was "?" and the true nature of the case is uncertain.)

Fatty change in the liver is a very common post-mortem finding, and consequently the question of the specificity of the liver lesion in the acute fatty liver of pregnancy is bound to be complex. However, the foamy appearance of the liver cells is quite unlike the usual appearance of a fatty liver cell in which the cytoplasm is filled but not necessarily enlarged by a few large globules of fat. This foamy change is a very uncommon finding in routine post-mortems, and there are good grounds for regarding it as a specific lesion when it is associated with the characteristic clinical syndrome. Sheehan (1940) remarks that he has seen a similar appearance in the livers of 3 cardiac patients who died some 2 or 3 weeks after delivery, but who did not develop jaundice. On the other hand, the mild fatty change that sometimes occurs in the liver in association with hyperemesis and with vomiting of late pregnancy (Sheehan, 1939) is different; this is a minor example of the ordinary fatty liver such as occurs following, say, a chronic anaemia.

Some explanation is necessary to account for the different morphologic appearances of the liver in the present disease. They are not related to the total amount of fat in the liver. Leevy *et al.* (1953) illustrate the appearances of fatty livers from chronic alcoholic patients. The livers contained different amounts of fat; in the liver containing 80 per cent of fat almost every liver cell contained a single globule of fat and, even in the livers containing less than 10 per cent of fat, the fat is distributed in isolated cells and each cell is filled with a single globule.

An alternative explanation, that the different morphology of acute fatty liver is related to the speed of the change, seems perhaps to be more convincing. Best, Hartroft and Sellers (1952) state that in the experimental fatty change in the liver of rats due to choline deficiency, in which fat accumulates very rapidly, stainable lipoid first appears as small intracellular globules and these coalesce to form spherical masses. It is possible that the foamy appearance in the present cases is due to the rapidity of the fatty change. However, whilst the clinical syndrome is undoubtedly acute, there is no information on the actual duration of the liver change.

Clinical Pathology

From all sources there is but little information on the clinical chemistry of this syndrome. For this reason a definite picture of the clinical chemistry cannot be given and the following attempt at such a picture is only tentative.

Blood Urea. In all 4 cases of the present series the blood urea was raised except when the patient was obviously recovering. The rise may be found as early as the 1st or 2nd day of the disease and reaches a level of about 120 mg./100 ml. some days later. Stander and Cadden's case (1934) also had a raised blood urea as did Case 2 of Dill (1950), but the recovery case recorded by Whitacre and Fang (1942) had a value of only 36 mg./100 ml. It is possible that, since most of the cases were clinically severe, the rise in the blood urea may be of some diagnostic importance; in acute massive hepatic necrosis the blood urea tends to fall (Zondek and Bromberg, 1947). In many cases of the present type it appears that, even when the clinical condition is severe, the liver retains the function of urea synthesis.

There is little information from proven cases on the amino-acid excretion; both Stander and Cadden and Whitacre and Fang report an increase of the blood amino-acid in their cases. A single estimation of the urinary ammonia on the 4th day in Case 3 showed a normal value and at this time the patient was in coma.

Liver Function Tests. Only two cases (3 and 4) of the present series provide biochemical data on liver function, apart from the level of serum bilirubin. In Case 3 there is a further complication in that 40 minims of chloroform were given at delivery. This raises the possibility that the chloroform might have modified the biochemical findings. This explanation is not thought likely for the following reasons: (*a*) at delivery no medical or obstetric abnormality was found other than the death of the baby; in particular there had been no vomiting; (*b*) labour was short, being of 8½ hours duration. With this clinical state prior to delivery it is most unlikely that the small amount of chloroform could have produced any liver change other than possibly an isolated liver cell lesion (Sheehan, 1940).

In both cases there was a normal thymol turbidity test and a raised serum alkaline phosphatase value shortly after the appearance of jaundice. In Case 4 the serum alkaline phosphatase value fell with increasing severity of the clinical condition. Repeat estimations of the serum alkaline phosphatase were not carried out in Case 3. In Dill's fatal Case 6 (1950) a normal thymol turbidity was also recorded at the 8th day of the disease.

The various biochemical findings suggest that the jaundice is obstructive in nature but that the obstruction is partial and is accompanied by damage to the liver cell.

Serum Potassium. In Case 2 a consistently low serum potassium value was found, varying from 3·3 meq. to 3·7 meq./litre. The association of liver damage with hypopotassaemia has been noted previously; Artman and Wise (1953) found hypopotassaemia in chronic alcoholics who showed evidence of acute hepatocellular damage either in early cirrhosis or in the course of a chronic cirrhosis. Latner (1950) also reported low serum potassium levels (10·9 and 12·3 mg. per 100 ml.) in 2 cases of massive hepatic necrosis one of which was designated

massive necrosis of the puerperium. However, the serum potassium level in Case 4 was normal and therefore hypopotassaemia is not a constant finding.

The cause of the hypopotassaemia is of some interest. Artman and Wise (1953) state that vomiting may account for losses of 5·0 to 7·0 meq. of potassium per litre of vomitus. This source of loss could well be operative in the present Case 2.

Of the possible causes for the low serum potassium levels, one is of peculiar importance since it concerns therapy. Intravenous glucose will lower the serum potassium level as a result of the formation and storage of glycogen in the liver. It could be argued that liver storage of glycogen is evidence of returning liver function and therefore of clinical recovery; hypopotassaemia would if such were the case be a hopeful finding, always provided that it were recognized and treated in time. However, there is too little information to be certain of the prognostic significance of a low serum potassium.

Hypoglycaemia. It is well known that failure of the glycogenic function of the liver may produce hypoglycaemia and with it convulsive attacks. Such attacks occurred in the case of Stander and Cadden (1934), and of Whitacre and Fang (1942). Unfortunately no estimations of blood sugar were made in the present cases.

Plasma Proteins. Nixon *et al.* (1947) say that, in a jaundice of short duration, an inversion of the albumen/globulin ratio suggests jaundice of pregnancy rather than infective hepatitis. As against this, Zondek and Bromberg (1947) found a reversal of the albumen/globulin ratio in severe cases of infective hepatitis. It is doubtful therefore, whether the estimation of plasma proteins would be of great diagnostic value in the severe case of acute liver failure.

The Relation Between the Liver Morphology and the Clinical Chemistry

From the preceding section it is seen that some of the biochemical findings suggest obstruction, although in the fatal cases no obstruction is found in the extrahepatic biliary system, and the pancreas is normal. Nevertheless, the jaundice may well be truly obstructive in type in that, although the larger biliary system may be patent, there is blockage to the finer bile channels in the lobule. In the description of the liver pathology it was noted that bile thrombi were found most prominently in the canaliculi of the centre parts of the lobule, less so in the periportal region and not at all in the portal tracts. One speculation is that the rapid accumulation of fat bloats the cells so much that the finer intracellular and intercellular bile channels are blocked—in other words there is a hepato-cellular obstruction. A similar explanation has been offered to account for the obstructive character of the jaundice in infective hepatitis. Himsworth (1950) believes that swelling of the liver cells and consequent impediment to the intralobular circulation may account for centro-lobular necrosis which follows many different causes. These explanations are, however, still hypothetical.

Whether the accumulation of fat in the liver cells can produce liver-cell dysfunction is difficult to determine. Some information can be gleaned from those reports dealing mainly with acute fatty liver in association with chronic alcoholism. Leevy *et al.* (1953) deal at length with the appearances and effects of the fatty liver of "large globule" variety in chronic alcoholics. Necrosis was not a feature in their cases, but jaundice occurred in 37·5 per cent of those with severe fatty liver change (i.e., with 80 per cent of fat in the liver) and they suggested that compression of the finer bile capillaries by extracellular fat could be responsible. A transient slight rise of the non-protein nitrogen occurred in some of the patients, albuminuria was found in about half of them and hypoglycaemia occurred in 2 cases. These authors state, however, that there was no correlation between the amount of liver fat and the results of the biochemical tests of liver function, and this would suggest that the liver dysfunction was not entirely due to fatty accumulation. Popper *et al.* (1953) in a similar series of cases of alcoholism with a non-cirrhotic fatty liver and severe jaundice also found clinical evidence of liver cell damage; the thymol turbidity was normal and there was a significant elevation of the alkaline phosphatase. They state that a centrolobular necrosis was present in all their cases and suggest that the cause of the acute liver damage

was a toxic hepatitis grafted upon a fatty liver whose resistance to minor infections and intoxications was reduced. On the other hand, Graham (1944) described 5 cases of sudden death in chronic alcoholics in which the only pathological lesion was a marked fatty change. He did not decide the actual cause of death, but suggested that a vitamin deficiency might have been responsible. Hypoglycaemia was ruled out in one case, but the levels of serum potassium were not estimated. All the cases died without jaundice and without any evidence of acute liver failure.

There is thus no agreement from these reports as to whether accumulation of fat can produce liver cell failure if there is no necrosis.

Cause of the Liver Lesion

The causes of any fatty accumulation in the liver can be grouped as follows: (1) dietary deficiencies, (2) hormonal imbalance states, as in diabetes, (3) oxygen lack, either due to anaemia or to ischaemia and (4) toxic or infectious processes. From the clinical evidence neither the present cases nor those in the literature were diabetics. Furthermore, anaemia of any degree is not a constant feature and no cause for ischaemia was observed in any of the autopsy cases.

Neither in the present cases nor in any of the cases from the literature is there any hint of chemical poisoning, prior to the onset of the disease. There is no evidence to suggest any known infectious process; in particular, investigations for leptospirosis in the first 3 cases proved negative, and the liver pathology is quite unlike that of viral hepatitis. Nevertheless, it is quite impossible to exclude the possibility of some unknown infectious agent whose action is sufficient to prevent function of the liver cell but not sufficient to kill the cell.

The conditions governing fatty infiltration of the liver in the experimental animal have been the subject of much study in recent years, notably by Best and his colleagues. The subject has been fully reviewed in the many publications of the above observers and also by Himsworth (1950).

It is established that one way in which fatty infiltration of the liver can be produced is by a diet deficient in factors which normally prevent the accumulation of fat there. Such preventive substances are known as lipotropes, the best known of which is choline, though certain proteins have the same effect: casein, egg white and beef muscle. It has been accepted that the active component in protein is methionine, the methyl group of which is used in the synthesis of choline. Other substances such as vitamins seem to control fat metabolism in the liver; thiamine is said to be necessary for the development of the fatty liver due to choline deficiency, riboflavin deficiency is reported to lead to gross fatty infiltration, and pyridoxine, too, may exert a lipotropic action.

Unfortunately there is no unequivocal parallel in human pathology to this experimental fatty infiltration. There is, however, a firm suspicion that a condition of prolonged fatty infiltration precedes diffuse hepatic fibrosis in man and that this fatty infiltration is probably the result of a lipotrope deficiency.

It is tempting, therefore, to consider whether acute fatty liver of pregnancy may be an example of such a lipotrope deficiency. There is no direct evidence in support of this hypothesis; in too few of the recorded cases is there any information about the previous diet of the patients, and all that can be said on this point is that none of the cases were chronic alcoholics and that none of them were starving.

If there were a lipotrope deficiency, this could arise either exogenously as a result of a poor protein diet or endogenously from an inability to utilize normal supplies of lipotropes. This inability might be due to some unknown toxic or infectious process which could interfere with the liver cell enzyme systems concerned with fat transport and fat metabolism.

The main objection to the theory of lipotrope deficiency is that, though there is gross fatty change in the liver both in experimental lipotrope deficiency and in the present disease, evidence of liver failure is negligible in the former but gross in the latter.

Treatment

On the idea that a lipotrope deficiency might at any rate play some part in causing the disease an attempt at specific therapy was made in

Cases 2, 3 and 4. Case 1, a fatal case, did not receive lipotropic agents but Case 4, also a fatal case, received intravenous methionine. In Case 2, 10 g. of choline chloride were given intravenously in glucose over a period of 24 hours. This patient recovered but it is more than likely from the clinical assessment that this patient would have recovered spontaneously. Case 3 was given intravenously not only 10 g. of choline chloride but also a mixture of amino-acids. The rationale of the latter addition is as follows: it is known that fatty change in the human liver may not respond to choline or to certain other lipotrope factors. Waterlow (1948) did not observe any dramatic beneficial effect from the treatment of fatty liver disease of infants with methionine, choline, or inositol. Furthermore, other non-sulphur-containing amino-acids such as threonine and lysine are reported to have lipotrope activity (*Nutrition Reviews*, 1954), and the possible effects of other amino-acids are not known. The fact that Case 3 recovered after a very severe illness is not proof that the above therapy was in fact responsible since spontaneous recovery can occur. Furthermore Case 4 died although she had received intravenous methionine. It could be argued that this patient was unable to utilize amino-acids and therefore might have responded better to choline, but it is also possible that some other lipotrope agent would have been effective.

The results are not wholly disappointing and it seems worthwhile to pursue, in future cases, the possible effects of lipotrope agents. Any such therapeutic effects may well be marred by the occurrence of hypopotassaemia, of hypoglycaemia, or of haemorrhage due either to prothrombin deficiency or fibrinogen deficiency, all of which may occur in acute liver failure. Such specific changes would of course need to be corrected by intravenous potassium solutions, intravenous glucose and fresh blood.

Recovery. Most of the cases recorded in the literature were fatal. The question of recovery is therefore pertinent. Unfortunately, apart from the 2 in the present series, there is only 1 proven case which recovered and this was recorded in detail by Whitacre and Fang (1942). It would seem reasonable to suggest that recovery from the acute fatty liver of pregnancy is more common than the paucity of such reports would indicate. There are many records of cases, designated as acute yellow atrophy or as massive liver necrosis of pregnancy or the puerperium, which recovered but in which a liver biopsy was not performed. Furthermore, Case 2 of the present series was milder than the usual case and as already emphasized would probably have recovered spontaneously; it can be assumed that similar mild cases occur which are not diagnosed or perhaps are not admitted to hospital. Needless to say, the possibility of spontaneous recovery makes the evaluation of methods of treatment very difficult.

Cases 2 and 3 have been seen at 1 year and at 7 months respectively following their illness. Both were quite well and had had no further trouble since discharge from hospital; they declined to come into hospital for follow-up studies.

Note. The term "acute yellow atrophy", has acquired two different meanings. In the first place it is used as a pathological term synonymous with acute massive hepatic necrosis and in the second to describe the clinical syndrome of acute liver failure. In the present disease acute yellow atrophy is obviously a term to be avoided even though prefixed by the word "obstetric", since it might be misinterpreted as having reference to the pathological meaning. The title "acute fatty liver of pregnancy" has therefore been introduced here; it is descriptive and carries with it no aetiological bias.

Summary

Four cases of acute liver failure in pregnancy are described in which the sole pathological change is one of fatty accumulation in the liver and in which necrosis of liver cells does not occur. In the absence of a known toxic cause it is possible that the patient might benefit from lipotrope treatment. Of 3 cases treated on this principle 2 recovered but further therapeutic tests are required before either the aetiology of the disease or the clinical effect of lipotrope agents can be elucidated.

Acknowledgments

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A CRITICISM OF THE HYPOTHESIS OF PLACENTAL INSUFFICIENCY

BY

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PLACENTAL insufficiency is sometimes invoked as a determining factor in the onset of labour, in intra-uterine death of the foetus, and sometimes too in the toxaemias of pregnancy. In part this emphasis on the importance of the placenta as a dominant organizer of pregnancy is due to the ease with which it can be examined and studied at leisure, compared with the difficulty in examining and studying such a changing organism as the foetus itself.

Essentially the placenta is a foetal organ. To determine the question whether the placenta or the foetus is dominant does perhaps imply some circularity of reasoning, and clearly the foetus and placenta together form a closely integrated unit, but the course of several of the foetal diseases tends to show that it is the foetus itself that is the dominant. Such a view might even be said to be valid on *a priori* grounds alone. In foetal erythroblastosis, for instance, the placental lesions, although often severe, are clearly secondary to changes in the foetus itself. Those common cases of pregnancy toxaemia in which the foetus ceases to grow and in which further conservative treatment is useless also illustrate the point. The poor development of the cord in cases of toxaemia and premature labour has some bearing on the issue.

The hypothesis of placental insufficiency is best examined in connexion with the cause of the onset of labour at term. The problem is complex. Delivery at term is the end result of a sequence of events, all of them significant, and maybe the preferable term would be a field or lattice of events, for all the several factors determining labour, distension of the uterus, reflex influences, ecbolics and so on, are integrated and need an organizer. The timing of labour at term is quite precise; it is a strictly organized phenomenon. The placenta on the other hand is a relatively unorganized and simple tissue; at all events it is an organ that undergoes little or no temporal differentiation. For that matter all attempts to demonstrate any comprehensive innervation of the placenta have been unsuccessful. The temporal precision of normal labour can only be determined by tissues which are undergoing a corresponding temporal differentiation. Such a view leads to the hypothesis that the dominant cause of the onset of labour must be sought in the foetus itself. Labour is clearly a goal-directed activity.

The question arises what evidence is there to substantiate or instantiate this view. Certainly at the present time there is very little direct evidence, our knowledge of foetal physiology being still far from complete, but there is some collateral evidence.

In the first place the well-established incidence of postmaturity in the anencephalic foetus cannot be disregarded.

In the second place the work of Barcroft on the establishment of the mechanism for adult respiration at term, and that of Coghill on the full development of purposive movements at term have shown that these integrated activities, activities which necessarily mature at term, are mediated by the central nervous system of the foetus. It would be a breach of Occam's razor, *entia non sunt multiplacanda sine necessitatione*, to assume that the determination of the time of onset of labour is mediated by any other cause than that which determines the maturation of the two fundamental activities which are the normal pre-requisites of extra-uterine existence.

The change in the oxygen needs of the mature foetus is certainly a factor, but it would seem likely that this change is secondary, and Walker's work on the alteration in the oxygen dissociation curves of the foetus as term approaches could be held to exemplify the dominant role of the foetal nervous system in the determination of the onset of labour. The oxygen needs of a foetus which needs to cry on its own must be different from those of one still in the uterus.

There is one further piece of evidence whose full significance remains still to be determined. It concerns the foetal adrenal cortex. At the time of full-time birth the innermost cortical cells of the adrenal cortex reach their maximum development. This zone is usually absent in anencephaly. These cells disappear after birth and only the outer rim of the gland of the embryo undergoes progressive differentiation into the suprarenal cortex of the adult.

To recapitulate, there are a number of foetal activities and functions which mature together at term. Their integration depends upon the foetal nervous system. The only hypothesis that satisfies the *lex parsimoniae* is that the onset of labour is mediated by the same mechanism. The peak of growth of the innermost zone of the adrenal cortex at term and the absence of this zone in anencephalic foetûs would seem likely to be of significance. Placental insufficiency with the admitted lack of any precise temporal differentiation of the placenta, would seem inadequate to account for the onset of labour at term.

WHY PROLONG LABOUR?

BY

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TEN years ago I returned home from World War II to find that a new condition called "inco-ordinate uterine action" had appeared. It seemed to have some relation to an old and respected enemy whom I knew in my youth and ignorance as "uterine inertia". I have some misgivings over the partial abandonment of what I had regarded as a simple forthright term that meant precisely what it said.

Before considering the subject in detail, it may be useful to recall certain observations of historic interest on the subject of "prolonged labour" with which these states of "inco-ordination" are inevitably linked. Nearly 100 years ago Sir James Y. Simpson wrote (1871): "Wait to see what nature can *effect*, not what she can *endure*." "The maternal mortality attendant upon parturition increases in a ratio progressive with the increased duration of labour." "The mortality to the mother and infant is tenfold greater in labours prolonged beyond, than in labours terminated within, twenty-four hours; and the mortality to the mother and infant is fifty-fold greater in labours prolonged beyond thirty-six hours, than in labours terminated within the first two hours."

I cannot recall who coined the phrase "meddlesome midwifery", but since that time much confusion has arisen as to where "meddlesome midwifery" ends and "timely intervention" begins. Mother and child have been known to fall unhappily between these two stools.

The following statement also affected me profoundly. It related to 147 autopsies on women who died of "obstetric shock" and particularly does it relate to the "prolonged labour" group which produced no deaths in women delivered within two days. It reads: "In contrast there were 46 deaths from shock in patients left for 3, 4 or more days in labour then delivered with relatively little further trauma. Two factors, length of labour and trauma of delivery, both played their part but the importance of length of labour does not appear to be sufficiently recognized." There should have been enough writing on the wall to make it fall down when these words were written by Professor Sheehan (1948) in his classic paper on obstetric shock. A year later came another warning, from Queen Charlotte's Hospital, (MacRae, 1949) pointing out with sombre significance that for the previous ten-year period the maternal mortality rate was 4·7 per 1,000 and the foetal mortality rate 120 per 1,000 if labour was prolonged. The maternal deaths related to three cases when labour lasted 69, 126 and 145 hours respectively, during which time various forms of medical treatment such as sedatives, acetylcholine and pitocin were exhibited. Professor Eastman, of Baltimore, stated (1947): "Uterine inertia and prolonged labour, let it be emphasized, are not synonymous, because prolonged labour may be entirely normal and physiologic, provided that steady, if slow, progress is made. Uterine inertia, on the other hand, is complete, prolonged absence of progress in the presence of weak contractions." Ostry (1955) commenting on this, shrewdly observes: "While the above may be true, the clinical effects of delay on both the mother and foetus are hurtful, regardless of the cause."

It is useful to consider certain aspects of this entity called "inco-ordinate uterine action".

AETIOLOGY

Much has been written about the effects of age, parity, constitution, such as the "dystocia dystrophia" pattern, nervous and emotional

factors, the "fear of the unknown", over-distension of the uterus, uterine malformations, primary dysmenorrhoea, and lastly, possibly most important of all, disproportion. It still seems unwarrantable to regard "inco-ordinate uterine action" as a disease entity. It will be recalled from early student days of frog muscle experiments that muscle fibres contract in two ways—by isometric contraction, in which the muscle contracts without appreciable shortening, or by isotonic contraction where there is obvious shortening, and where the contraction and relaxation phases are shorter by comparison with the former type. It is suggested that the first stage of labour represents within the muscle fibres a combination of both types of contraction, with isotonic contraction predominating so long as steady progress continues. Whilst the membranes are still intact and should the foetal bulk be considerable, no great shortening of the fibres is, however, permissible. Ultimately, at full dilatation and expulsion of the infant and of the placenta the uterine fibres return to their resting length. It is further suggested that this so-called disease is no more than gross aberration of normal activity in which the predominant pattern of muscular activity is isometric in type rather than isotonic. Arrested progress of the presenting part and prolongation of labour are the inevitable accompaniments. This undesirable state of affairs may be properly described by the term "inertia" without need for the more extensive classifications recently suggested. At least the term "inertia" simplifies the outlook and, even more important, determines the conduct of the labour, making it active rather than passive, timely rather than meddlesome.

Reynolds and his co-workers (1954) have produced an impressive array of data relating to orderly and disorderly uterine action. Their observations, which are of great interest, are properly within the province of the experimental physiologist; the outlook of the practising clinician must be somewhat different. Despite the various agencies that may be expected to enhance the activity of the inefficient uterus no responsible clinician can minimize the devastating effects occasioned by the mere prolongation of labour in raising enormously the stillbirth and maternal mortality and morbidity rates. Further evidence of these risks may be inferred from recent studies on placental action using radioactive sodium, and it will be recalled that Johnson and Clayton (1955) pointed out that in many cases of prolonged labour there is a severe reduction of placental action, which in some instances may be as low as 50 per cent of the normal mean value. The importance of this in relation to foetal survival after many hours of ineffective labour cannot be over-emphasized.

Treatment

Reasonable sedation whilst steady if somewhat slow progress is still apparent, needs no further mention, though there appears to be no particular virtue in giving several hundred milligrams of so useful a drug as pethidine if it occasions a risk of overlooking the cessation of real progress.

Oestrogens are still being advocated, but it is doubtful whether they are of the least value. Theobald *et al.* (1948) gave an old drug a new look, but second thoughts upon the usefulness of the pitocin drip technique are now pervading the literature. It seems clear that its safe employment requires a full complement of resident staff. Tetra-ethyl ammonium chloride has been used, but Jeffcoate *et al.* (1952) found it of doubtful value, nor has much benefit been found to accrue from the use of di-hydroergotamine (Jeffcoate and Wilson, 1955). Of caudal analgesia I have no personal experience.

In the present state of knowledge, the place of surgical treatment alone remains to be considered. Nixon (1952) has described it as a mechanistic escape from a difficult situation, though the same criticism might be levelled at appendicectomy for acute appendicitis. It is not intended to make dogmatic statements as to the time beyond which true labour becomes prolonged, but to emphasize that the timing of surgical intervention remains a matter of paramount importance that must, when occasion demands, be detached from these fascinating studies in uterine physiology that are the rightful concern of the academician.

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OVULATION IN THE CONGENITAL ABSENCE OF THE UTERUS

BY

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AN excitable girl of Irish-Armenian parentage was seen at the age of 19 on account of primary amenorrhoea. Her only other complaint was of low backache and lower abdominal discomfort for about 4 days every month.

She was of average physique, being 5 feet in height and weighing 7 stones 6 pounds, and the secondary sex characters were normally developed. The pubic escutcheon, however, was of the male type, and indeed she was more hirsute than average, although not more so than is commonly seen in women in the Middle East.

General and abdominal examination were negative, but inspection of the vulva showed no vaginal introitus. The girl was therefore admitted to hospital for further investigation, it being thought possible that she had a haematometra associated with vaginal atresia. As Wolffian and Müllerian abnormalities often co-exist, an intravenous pyelogram was performed but it showed no abnormality. The daily output of 17-ketosteroids in the urine was 18 mg.

At examination under anaesthesia the absence of the vaginal introitus was confirmed. Rectally it felt as if the cervix and uterus were also absent, the anterior ends of the utero-sacral ligaments meeting in the midline. In addition there was a cystic swelling, the size of a billiard ball, in the right appendage region. It was considered that this might be the cause of her monthly pain, particularly if it were a haematometra in a non-patent right uterine horn.

Laparotomy was therefore performed, and the findings were as follows. There was no cervix, and the uterus was represented merely by two small nubbins of tissue separated from each other by a transverse fold of peritoneum about 2½ inches long. From the lateral aspect of each of these nodes there arose a poorly developed round ligament and also a normally formed Fallopian tube. According to Blair-Bell (1919), this combination of uterine aplasia and normal tubes is not uncommon. The right ovary was the seat of a dark blue cyst, 3 inches in diameter. The left ovary was normal and contained a recent corpus luteum. The cyst was resected from the right ovary and the corpus luteum from the left.

Microscopically the lining of the cyst, which contained old blood, was of fibrous tissue only, so that its origin remains obscure. The corpus luteum was adjudged about 14 days old.

The question of ovarian function after removal of the uterus is still debated, but most gynaecologists hold that such function may continue. In congenital absence of the uterus, the ovaries are usually present, and their normal endocrine function is reflected by the normal development of the secondary sex characters. The present case indicates that in such circumstances ovulation may also occur. I have found only a single reference to this point, in a monograph by Burch and Lavery (1954) on hysterectomy, where a similar finding at laparotomy is casually mentioned. There is evidence that in the present case ovulation was probably occurring regularly for near the corpus luteum were several corpora albicantes. Further, after her discharge from hospital the patient recorded her basal body temperature for 5 weeks, and the chart showed the temperature shift regarded as indicative of ovulation. At the end of the 5 weeks the patient and her family moved to Malta.

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STILLBIRTH AND NEONATAL MORTALITY IN TWIN PREGNANCY

BY

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AT the present day the human species is characteristically uniparous and twinning has come to be regarded as an atavism. It is well known that twin pregnancy involves greater risk of complications and of maternal and foetal death than does single pregnancy.

Many papers about twin pregnancy have been published in recent years, but relatively little attention has been given to the high death rates among the babies. For that reason the present review, which is mainly a study of the causes of mortality among twin infants, is presented.

MATERIAL

This is a study of 397 twin pregnancies among 388 women who booked for confinement at the Aberdeen Maternity Hospital and who were delivered between the years 1938 and 1952. Abortions (stillbirths before the 28th week of pregnancy) were not included in the series, but liveborn infants which were pre-viable (gestation period of less than 28 weeks) and which died after birth, were included.

During the 15-year period the work of the Maternity Hospital increased greatly. In 1938–40 only about one-quarter of the births in the City of Aberdeen were booked hospital patients, but this proportion rose to one-half in 1946 and to about three-quarters in 1949–52. If the period is divided into three 5-year groups, twin labours among booked cases in 1938–42 numbered 86, in 1943–47 131, and in 1948–52 180.

Probably a greater proportion of "bad risk" cases were selected and booked for hospital delivery during the earlier years of the survey. There is no way of determining the exact extent of this selection, which may well, however, have influenced changes in foetal mortality rates during the period of the survey.

INCIDENCE

The frequency of twin to single pregnancies during the period under review is 1:66. The general rate for Scotland over the period 1939–1952 was 1:72 (Registrar-General for Scotland). No attempt was made to classify uniovular and binovular twins separately, as the descriptions of the foetal membranes were not always complete; in any case, this method of differentiation is unreliable. Table I shows that the incidence of twinning increases with age and reaches its maximum in the 30–39 year group; increasing parity has a similar effect. This confirms the observations of Matthews Duncan (1864), McArthur (1953) and Stocks (1953).

According to Greulich (1934) and Guttmacher (1937), uniovular twinning is a chance phenomenon the incidence of which is unaffected by age, parity or race; whereas the incidence of binovular twinning varies markedly with race, increases with age and carries a hereditary tendency. Since binovular twinning occurs about three times as often as uniovular twinning, any series of twin pregnancies in which no distinction between the two types is made, will show, by and large, the characteristics of binovular twins.

TOTAL FOETAL MORTALITY

In earlier published series, foetal mortality varies from 39 per cent (Clarke, 1786) and 31 per cent (Guttmacher, 1939) to 11 per cent (Bender, 1952). It is difficult to assess the differences

TABLE I
Incidence of Twin to Single Pregnancy by Age and Parity
(Ratios are given only when based on more than two twin pregnancies)

Parity	Type of Pregnancy	Total	Age					
			15–19	20–24	25–29	30–34	35–39	40+
1st	Twin	129	17	44	44	14	9	1
	Single	11,720						
	Ratio	1 : 91	1 : 104	1 : 129	1 : 65	1 : 69	1 : 42	—
2nd	Twin	112	2	39	43	15	10	3
	Single	7,345						
	Ratio	1 : 66	—	1 : 64	1 : 62	1 : 89	1 : 50	1 : 33
3rd	Twin	71	2	9	21	29	10	—
	Single	3,569						
	Ratio	1 : 50	—	1 : 83	1 : 64	1 : 31	1 : 45	—
4th+	Twin	85	—	3	18	35	23	6
	Single	3,371						
	Ratio	1 : 40	—	1 : 75	1 : 50	1 : 31	1 : 36	1 : 55
Total	Twin	397	21	95	126	93	52	10
	Single	26,005	1,972	9,181	7,787	4,294	2,166	605
	Ratio	1 : 66	1 : 94	1 : 97	1 : 62	1 : 34	1 : 42	1 : 60

between one series of cases and another because of such confusing factors as the different definitions of stillbirths between Britain and the U.S.A., and between the different States of the latter country. Most studies have been made on hospital cases which are more or less selected. This source of bias has been diminished to some extent in the present series which includes only "booked" cases, emergency admissions being excluded.

Table II shows that in the present series the neonatal mortality has fallen steadily from 19·5 per cent in the 1938–42 group to 11·1 per cent in the 1948–52 group. The stillbirth rate, on the other hand, has changed little during this period.

While the variations in the mortality may be influenced to some extent by differing selection factors, the fall in neonatal mortality is too great and too uniform to be due solely to this and it is probably due in part to the better facilities for care of the newborn in the hospital since 1941. The national war-time food policy is believed to have been responsible for a nation-wide fall in stillbirths and neonatal mortality from almost all causes, and this no doubt helped to lower the mortality from prematurity in twin pregnancy (Duncan, Baird and Thomson, 1952).

Prematurity, as might be expected, was the largest determining factor in foetal mortality in this series. Hirst (1939), Munnell and Taylor

TABLE II
Stillbirth and Neonatal Mortality by Group

Quinquennium	No. of Births	Stillbirths		Neonatal Deaths		Papyraceous	Total Foetal Deaths	
		No.	Per cent Total Births	No.	Per cent Live Births	No.	No.	Per cent Total Births
1938–1942	172	8	4·7	32	19·5	—	40	23·2
1943–1947	262	14	5·3	38	15·4	1	53	20·2
1948–1952	360	14	3·9	38	11·1	4	56	15·5

(1946), Potter and Crunden (1941), Bender (1952) and Russell (1952) have stressed the relation of prematurity to the high foetal mortality in multiple pregnancy. It has not been possible to define the incidence of prematurity by dates in this series, as the duration of pregnancy was not accurately known in many cases. An analysis of birth weights (Table III), however, shows that, of the 794 infants, 465 (58·6 per cent) weighed 5½ pounds or less and so classify as premature by weight. Of these, 181 (22·8 per cent of the total) weighed 4 pounds or less, and these contributed 68 per cent of the deaths. This table also shows the close relationship between birth weight and both stillbirth and neonatal death rates.

Trends in stillbirths and neonatal deaths will now be considered in more detail.

Stillbirths

Prematurity, while not an immediate cause of stillbirth, is often a most important predisposing factor. In this series, there were 15 stillbirths in babies weighing 4 pounds or less at birth (8·3 per cent). In those between 4 and 5½ pounds in weight there were 14 stillbirths (5·0 per cent) while in those babies whose weights were over 5½ pounds, only 5 were stillborn (1·6 per cent). Two stillborn babies did not have their weights recorded. Of the 36 stillborn babies, 17 had been dead for some time before delivery and were macerated.

Table IV shows that in 10 cases stillbirth was due to the "hazards" of birth (27·8 per cent of the total twin stillbirths), and in 9 of these it was the second twin that was stillborn, suggesting that there is some scope for improvement in the management of delivery of the second twin. Fifteen (41·7 per cent) died from causes present before labour, and the remaining 11 stillbirths (30·5 per cent) were unexplained.

Neonatal Deaths

Table V shows 108 neonatal deaths classified by cause.

In 80 (74·1 per cent) the cause of death appeared to be principally prematurity. With one exception, these babies weighed less than 4 pounds and they have been classified according to the cause of the premature onset of labour rather than the immediate cause of death. These deaths were considered to be due primarily to

TABLE III
Stillbirth and Neonatal Mortality by Birth Weight

Birth Weight	Total Births		Stillbirths		No. of Livebirths	Neonatal Deaths		Total Foetal Deaths	
	No.	Per cent	No.	Per cent		No.	Per cent	No.	Per cent
1 lb. 1 oz.–1 lb. 8 oz. ..	7	0·9	1	11·1	6	6	100·0	7	100·0
1 lb. 9 oz.–2 lb. ..	11	1·4	1		10	10		11	
2 lb. 1 oz.–2 lb. 8 oz. ..	22	2·8	3	10·9	19	17	81·6	20	83·6
2 lb. 9 oz.–3 lb. ..	33	4·2	3		30	23		26	
3 lb. 1 oz.–3 lb. 8 oz. ..	44	5·5	3	6·8	41	19	46·3	22	50·0
3 lb. 9 oz.–4 lb. ..	64	8·1	4	6·3	60	11	18·3	15	23·4
4 lb. 1 oz.–4 lb. 8 oz. ..	71	8·8	3	4·2	68	7	10·3	10	14·1
4 lb. 9 oz.–5 lb. ..	99	12·5	5	5·1	94	4	4·3	9	9·1
5 lb. 1 oz.–5 lb. 8 oz. ..	114	14·3	6	5·3	108	2	1·9	8	7·0
5 lb. 9 oz.–6 lb. ..	108	13·6	2	1·4	106	1	1·4	3	2·8
6 lb. 1 oz.–6 lb. 8 oz. ..	103	13·0	1		102	2		3	
6 lb. 9 oz.–7 lb. ..	53	6·7	2		51	4		6	
7 lb. 1 oz.–7 lb. 8 oz. ..	34	4·3	0		34	0		0	
7 lb. 9 oz.–8 lb. ..	15	1·9	0	1·8	15	1	4·7	1	6·4
8 lb. 1 oz.–8 lb. 8 oz. ..	6	0·8	0		6	0		0	
8 lb. 9 oz.–9 lb. ..	1	0·1	0		1	0		0	
Unknown	4	0·5	2	—	2	1	—	3	—
Papyraceous	5	0·6	—	—	—	—	—	5	—
Total	794	100·0	36	4·5	753	108	14·3	149	18·8

TABLE IV
Stillbirths by Cause

Unknown		Factors Existing before Labour			Hazards of Labour		
1st Twin	2nd Twin		1st Twin	2nd Twin		1st Twin	2nd Twin
		Eclampsia	1	2	Delay in delivery of 2nd Twin	–	2
		Pre-eclampsia	1	2	Prolapsed cord	1	4
		Ante-partum haemorrhage	1	2	Separation of placenta ..	–	3
		Foetal deformity	–	1			
		Late vomiting	1	–			
		Hydramnios	2	2			
6	5		6	9		1	9
11			15			10	

TABLE V
Cause of Neonatal Death in 108 Babies

Premature Babies						Mature Babies	
Death Due Mainly to Prematurity			Death Due to Factors Other than Prematurity				
Cause of Premature Labour	No.		Cause of Death	No.		Cause of Death	No.
Pre-eclamptic toxaemia ..	13		Infection	9		Infection	2
Eclampsia	1		Intracranial haemorrhage ..	6		Intracranial haemorrhage	2
Ante-partum haemorrhage	3		Deformity	3		Deformity	2
Late vomiting	3		Haemorrhagic disease ..	1		Bilateral pleural effusion of unknown cause	1
Hydramnios	8		Jaundice of unknown cause	1		Unexplained	1
Debility	12						
Other	5						
Unknown	35						
Total	80			20			8

the immaturity of the baby, whether the mode of dying was asphyxia from poorly expanded lungs or from regurgitation of feeds, or from infection which was not likely to have been fatal to a more mature baby. In 20 (18·5 per cent) the babies, although premature (less than 5½ pounds in weight), did not die as a direct result of prematurity, and these deaths were therefore classified according to the apparent cause. Infection, cerebral haemorrhage and deformity were the commonest causes in this group. Deaths were due to similar causes in the 8 (7·4 per cent) mature babies.

The fall in neonatal mortality through the period of study was not due to a decrease in the incidence of prematurity since the percentage of liveborn infants weighing 4 pounds or less in the three 5-year periods between 1938–52 was 18·9, 27·0 and 19·7 respectively. Table VI shows that a marked fall in mortality occurred between periods 1938–42 and 1943–47 among infants of all birth weights, but little further decrease occurred in the period 1948–52.

The figures given below show that the decrease in mortality has been mainly among those babies that died after the first 48 hours.

	Death within 48 hours	Death over 48 hours
1938–42	17 (10·4 per cent)	15 (9·2 per cent)
1943–47	30 (12·1 per cent)	8 (3·2 per cent)
1948–52	29 (8·5 per cent)	9 (2·6 per cent)

Since deaths after 48 hours are most often due to infections acquired after birth, it looks as if better medical and nursing care and the use of

TABLE VI
Distribution of Neonatal Deaths Among 753 Live Births by Birth Weight and Group

Quinquennium	Birth Weight										
	4 pounds and under			4 pounds 1 ounce to 5 pounds 8 ounces			Over 5 pounds 8 ounces			Unknown	
	No.	Neonatal Deaths		No.	Neonatal Deaths		No.	Neonatal Deaths		No.	Neonatal Deaths
		No.	Per cent		No.	Per cent		No.	Per cent		No.
1938–1942 ..	31	23	74·2	61	6	9·8	72	3	3·9	—	—
1943–1947 ..	67	34	49·2	99	3	3·0	81	1	1·1	—	—
1948–1952 ..	68	29	42·6	110	4	3·6	162	4	2·5	2	1
Total 1938–1952	166	86	51·8	270	13	4·8	315	8	2·5	2	1

antibiotics were largely responsible for the improvement. In 1941, the Aberdeen Maternity Hospital increased the size of its nursery for premature and ill babies, and a special whole-time staff was employed. Since then, the incidence of infection within the nursery has fallen, and fewer deaths have occurred among the premature babies generally. Although it is gratifying to note this improvement, it is obvious that most neonatal deaths in twins result primarily from prematurity, and that any further appreciable saving of lives among these babies must depend upon a reduction in the number of premature labours.

CAUSE OF PREMATURE LABOUR IN TWIN PREGNANCIES

Since prematurity is such an important cause of the high foetal mortality in twins, it is important to enquire into its cause with a view to prevention.

In some cases labour was induced, but in most premature labour began spontaneously. As the information in some of the earlier records was incomplete, the cases for the last 5-year period only (1948–52) were used for this part of the analysis. Of the 180 cases, labour began spontaneously in 139, and was induced in 40; one pregnancy was terminated by an elective Caesarean section. In 29 (20·2 per cent) of the cases in which labour began spontaneously, the combined weight of the babies was 8 pounds or less, and in only 1 (2·8 per cent) of those in which labour was induced. Most of the small premature babies, therefore, result from premature labour of spontaneous onset.

COMPLICATIONS OF PREGNANCY

It is well known that maternal complications are commonly associated with plural pregnancy, and it was thought that this might have some relation to the frequency of premature labour.

Table VII shows the occurrence of complications of pregnancy in 397 pregnancies related to the combined birth weights of the babies (weight here being taken as an index of prematurity). Three weight groups were arbitrarily selected—8 pounds and under, 8 pounds 1 ounce to 10 pounds, and over 10 pounds. Where more than one abnormality of pregnancy existed the case was placed in the group of the complication which seemed most likely to affect the birth weight of the babies.

In 47 per cent of all cases, no significant complications of pregnancy could be found, and this figure varied little between the three weight groups.

PRE-ECLAMPSIA AND ECLAMPSIA

Of the 397 pregnancies in the present series, 132 (33·3 per cent) were complicated by varying degrees of pre-eclampsia. This includes 10 mild cases classed in Table VII under other headings.

It is not possible to compare the incidence of pre-eclampsia with those of other series as the definition of what constitutes pre-eclampsia varies greatly. In any case its incidence is affected by age and parity which would have to

TABLE VII

Incidence of Complications of Twin Pregnancy According to the Combined Birth Weights of the Babies

Complication of Pregnancy	Combined Birth Weight							
	8 pounds or less		8 pounds 1 ounce to 10 pounds		Over 10 pounds		Unknown and Papyraceous	Total	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	No.	Per cent
None	37	50·7	42	45·2	106	47·5	2	187	47·1
Pre-eclampsia (mild and moderate)	6	8·2	23	24·7	68	30·5	1	98	24·7
Pre-eclampsia (severe)	6	8·2	6	6·5	5	2·2	1	18	4·5
Eclampsia	—	—	3	3·2	3	1·3	–	6	1·5
Hypertension	2		3		4		–	9	
Ante-partum haemorrhage	4		1		1		–	6	
Hydramnios	5		5		7		2	19	
Late vomiting	2	32·9	–	20·4	–	18·5	–	2	22·2
Pyelitis	1		–		–		–	1	
Debility	7		5		21		–	33	
Miscellaneous	3		5		8		2	18	
Total	73	100·0	93	100·0	223	100·0	8	397	100·0

be allowed for before any valid comparisons could be drawn. In this series three grades of pre-eclampsia were recognized:

(1) *Mild.* Slight elevation of blood pressure above 130/90 with minimal or no albuminuria. Most were admitted to hospital for varying periods of time but some were not.

(2) *Moderate.* Higher blood pressure with oedema and albuminuria (up to 2 g. per litre).

(3) *Severe.* Requiring urgent treatment or induction, blood pressure high and albuminuria more than 2 g. per litre.

(4) *Eclampsia.*

Among primiparae, pre-eclampsia occurred in 52 per cent of twin pregnancies compared to 23·7 per cent of single pregnancies. In the twin group, the incidence of mild, moderate and severe pre-eclampsia was 26·4, 11·6 and 7·0 respectively, and among the single pregnancies 19·3, 2·3 and 1·5 respectively. Therefore, although mild pre-eclampsia is only slightly more common in twin pregnancy, the more severe grades are about 5 times as common as in single pregnancies.

Of the 132 cases of pre-eclampsia associated with twin pregnancy, 88 were mild, 20 moderate, and 18 severe, and in 6 eclamptic fits occurred. The foetal mortality associated with mild or moderate pre-eclampsia was 9·0 and 10·0 per cent respectively and with severe pre-eclampsia and eclampsia 27·8 and 25·0 per cent. The 24 pregnancies complicated by severe pre-eclampsia and eclampsia accounted for 8·7 per cent of the total foetal deaths.

Despite the high foetal mortality associated with severe toxaemia the overall foetal mortality in twin pregnancies complicated by pre-eclampsia of all grades of severity is considerably less (12·5 per cent) than among the pregnancies not complicated by pre-eclampsia (21·9 per cent). Although one-third of all the twin pregnancies were complicated by some degree of pre-eclampsia, only one-fifth of all stillbirths and neonatal deaths occurred in this group. Possibly this is because pre-eclampsia, as a rule, does not develop till fairly late in pregnancy when the risk to the child of extreme prematurity is past.

HYDRAMNIOS

The reported incidence of polyhydramnios in twin pregnancies varies from 24 per cent (McIlroy and Evans, 1927) to 2·1 per cent (Potter and Crunden, 1941), but much of this variation results from lack of agreement as to what constitutes excess liquor amnii.

Twenty-three cases of hydramnios occurred in this series, an incidence of 5·8 per cent. Seventeen were mild, and among these there were 2 stillbirths and 4 neonatal deaths. Six were severe; labour began spontaneously in 2, in 1 labour was induced surgically, and, in the remaining 3, labour began shortly after abdominal paracentesis was performed. There were 3 stillbirths and 6 neonatal deaths among the severe cases (75 per cent), due principally to extreme prematurity.

Other complications of pregnancy were too infrequent in this series to make it possible to discuss them individually.

Influence of Antenatal Rest in Hospital

It has already been mentioned that, in cases of pregnancy complicated by pre-eclampsia, many of the babies were of a reasonable size. Many of these patients had been in the antenatal wards of the hospital for some time, and it was thought that the prolonged rest in bed might have delayed spontaneous onset of labour until fairly near term. The incidence of premature onset of labour was therefore studied in three groups:

Group A (262 pregnancies) consisting of all patients who had not been admitted to hospital antenatally. Rest in bed before the 28th week of pregnancy or for periods of less than 7 days was ignored as unlikely to have much effect on the pregnancy.

Group B (102 pregnancies): patients admitted to hospital for a minimum of 7 days, because of a well defined abnormality such as pre-eclampsia. Where a patient was admitted more than once after the 28th week, the lengths of the periods of rest were added together.

Group C (33 pregnancies): patients admitted to hospital with no clearly defined complication other than "debility" or merely for rest because of the twin pregnancy.

In all groups, the combined weight of the babies at birth was related to the length of stay in hospital, and the results are shown in Table VIII. It might be expected that the benefit of rest in bed would be shown most clearly in those admitted to hospital because of debility and twin pregnancy, and, as the table shows, a higher percentage of the babies in Group C are big. It is, however, doubtful if this is a clear case of cause and effect. In about 20 per cent of cases the gestational periods were not accurately known, but, of the remainder, about 60 per cent in Group B and 45 per cent in Group C were admitted after the 35th week, by which time the danger of extreme prematurity is past. It may indeed be that many of the patients developed symptoms necessitating admission to hospital because the babies were so big as to make it difficult for them to walk around.

If rest in bed is to contribute substantially to the lowering of foetal mortality, admission to hospital would have to be arranged, as suggested by Bender (1952) and Russell (1952), not later than the 30th to 32nd week of pregnancy.

Table VIII
Effect of Rest in Hospital on the Combined Birth Weight of the Babies
(See text for description of Groups)

Group	Total Pregnancies	Combined Birth Weight of 10 pounds or less		Combined Birth Weight of over 10 pounds		Birth Weight Unknown	
		No.	Per cent	No.	Per cent	No.	Per cent
A (no rest)	262	128	48·8	129	49·3	5	1·9
B (7–20 days' rest) ..	73	25	34·2	46	63·0	2	2·8
B (21+ days' rest) ..	29	8	27·6	20	69·0	1	3·4
C (7–20 days' rest) ..	16	3	18·7	13	81·3	–	—
C (21+ days' rest) ..	17	2	11·8	15	88·2	–	—
Total	397	165		223		8	

Influence of Method of Delivery on Foetal Mortality

In the group weighing less than 4 pounds the mortality is high even after easy spontaneous delivery, since prematurity, rather than the mode of delivery, is the determining factor. In the other weight groups, the method of delivery does not appear to influence the death rate, except for delivery of babies weighing between 4 and 5½ pounds by version and extraction; 3 out of 12 such babies were stillborn. Since this operation was usually performed only when an urgent indication, such as prolapsed cord or marked foetal distress, was present, and where forceps delivery was not feasible, the mortality may not be due wholly to the manipulation. In any case, the number of babies involved is small.

It is therefore concluded that the size of the baby is of far greater importance than the method of delivery in determining its chance of survival.

Influence of Maternal Height

Baird (1949) has demonstrated a relationship between the height of the mother and the weight of the baby, the foetal mortality and the prematurity rate. There are very few small women (5 to 10 per cent) where the father belongs to the highest economic group (Registrar General's Social Classes I and II), but there are many more (25 to 30 per cent) among the lowest economic group (Social Class V). Within each Social Class, and especially in the lower income group, tall women appear to be healthier and have lower stillbirth rates than the small women. It seems clear that many small women in Britain are small not for reasons of heredity but because of the effect of faulty environment in youth which has impaired growth. The greater strain of twin pregnancy might be expected to exaggerate these differences between tall and short women.

Since 1944 the height of practically every patient delivered in the Aberdeen Maternity Hospital was recorded, and in this series the heights were known in all but 23 of the 622 patients delivered in 1943–52. Three maternal height groups were used—below 5 feet 1 inch (small), 5 feet 1 inch to 5 feet 3¾ inches (medium), and 5 feet 4 inches and over (tall).

Among 96 primiparae having a twin pregnancy, there were 17 small, 47 medium and 32 tall women, and over the same period of time 1,928 small, 3,994 medium and 2,077 tall women had single pregnancies, so that the ratio of twin to single pregnancies was 1:113 in the small women, 1:85 in those of medium height, and 1:65 in tall women. The higher incidence of twinning in tall women may be due to chance, or it may be that tall women have a higher twin conception rate or a lower twin abortion rate than smaller women. Any of these explanations would be difficult to prove. It would be helpful if the pregnancies could be separated into uniovular and binovular, as it is known that, in man, uniovular twinning is constant in all sections of the community, whereas binovular twinning varies according to race, age and other factors. Thomson (1949) has shown that, in sheep, where twinning is almost entirely binovular, the ewes that produced twin lambs were, on the average, heavier and larger before conception than those which produced single offspring. It has also been shown by White and Fraser Roberts (1927) that, in sheep, the incidence of twinning can be raised or lowered by an improvement or deterioration in the pasture. When ewes were kept on poor mountain grazings, only 1·7 per cent produced twins but when ewes of the same breed were kept on cultivable farm land, the proportion rose to 32·0 per cent. It may be that in man, where two-egg twinning is three times as common as one-egg twinning, the taller and better nourished women may, like the sheep, be more likely to produce binovular twins.

Tchouriloff in 1877 estimated the incidence of twinning in the various administrative districts of France, Italy, Bavaria and Roumania, and related this to the height of the population as measured by the proportion of men exempted from military service on account of short stature. He found that twinning was most frequent in the areas where the exemptions on account of short stature were fewest.

Torgensen (1951) also found that the incidence of twinning was high in East and Central Norway where the average stature of the popula-

TABLE IX
Stillbirth and Neonatal Death Rates by Height
(288 Patients)

Height	Total Births	Stillbirths		Neonatal Deaths		Papyraceous	Total Loss	
		No.	Per cent	No.	Per cent	No.	No.	Per cent
Small	130	7	5·4	28	21·6	1	36	27·7
Medium	280	12	4·3	27	10·4	3	42	15·0
Tall	166	5	3·0	14	8·8	1	20	12·1

TABLE X
Foetal Loss by Weight and Maternal Height

Birth Weight	Small			Medium			Tall		
	No.	Stillbirths and Neonatal Deaths		No.	Stillbirths and Neonatal Deaths		No.	Stillbirths and Neonatal Deaths	
		No.	Per cent		No.	Per cent		No.	Per cent
1 pound 1 ounce–2 pounds ..	7	7	95·2	3	3	85·9	3	3	93·4
2 pounds 1 ounce–3 pounds ..	14	13		11	9		12	11	
3 pounds 1 ounce–4 pounds ..	27	9	37·0	41	10	24·4	12	2	16·6
4 pounds 1 ounce–5 pounds ..	23	5	21·8	64	5	7·8	31	1	3·2
5 pounds 1 ounce–6 pounds ..	36	—	—	76	5	6·6	52	2	3·8
6 pounds 1 ounce–7 pounds ..	18	1		64	5		36	—	
7 pounds 1 ounce–8 pounds ..	4	—	4·5	16	1	7·4	15	—	—
8 pounds 1 ounce–9 pounds ..	—	—		1	—		4	—	
Unknown	—	—	—	1	1	—	—	—	—
Papyraceous	1	1	—	3	3	—	1	1	—
Total	130	36	27·7	280	42	15·0	166	20	12·2

tion was greatest, and was low in the northern provinces where the population had a lower average height.

If the incidence of twinning is indeed related to maternal height, one might expect a social class gradient, since Social Classes I and II contain a larger proportion of tall and well nourished women than do Social Classes IV and V. No such gradient, however, can be observed in the 1949 figures for England and Wales (Daly, 1954). Unfortunately Daly was not able to break down his figures by parity. The lower social classes contain a higher proportion of multiparae and, since twinning increases with rising parity, it may be that the social and parity factors cancel each other out. Only a simultaneous analysis by age, parity and social class would show whether good economic status increased the likelihood of twinning.

There is no doubt, however, that the foetal mortality in twins is less among tall than among short women. Table IX shows that in this series it was 27·7 per cent in small women and 12·1 per cent in tall women. The difference is most marked in the neonatal death rates.

Since the foetal mortality in twins has already been shown to be intimately related to birth weight, it was to be expected that tall women will have larger babies than small women. Babies of aggregate weight less than 8 pounds occurred in 32·3 per cent of small women, 16·4 per cent of medium, and 13·2 per cent of the tall women. Babies weighing over 10 pounds in aggregate occurred in 41·5, 59·3 and 67·5 per cent of these respective groups. Over 10 per cent of the tall women had babies which together weighed over 14 pounds, but none of the short women achieved this.

The foetal mortality in the three maternal height groups shows no appreciable difference for infants weighing 3 pounds or less. Between 3 and 5 pounds, the mortality is 7 per cent

among the babies of tall women, and 28 per cent among those of small women. It may be that the premature babies of tall mothers have more vitality than those of smaller women. Among babies over 5 pounds so few die that no comparison between those of the different height groups is possible.

At equivalent gestational periods, the difference in mean birth weights between babies of tall, medium and small women is very small, and, as the death rates in babies of tall women are less, it suggests that these babies survive because of better vitality. Tall women as a group produce bigger babies than small women, due apparently to their ability to avoid premature labour longer than the smaller women. McKeown and Record (1954) made similar observations in Birmingham where they found that the gestational period and birth weight increased with maternal height in twin pregnancy but not in a singleton pregnancy. It is possible that the tall women have a larger uterus and a larger abdominal cavity so that there is less likelihood of excessive pressure as pregnancy advances. While such factors may play a part, it seems probable that, in the City of Aberdeen at least, the superior health and nutrition of the tall women make them better able to stand the strain of a twin pregnancy.

Discussion

It has been shown that, in the Aberdeen Maternity Hospital, between the years 1938 and 1952 the stillbirth rates in single and twin pregnancies were 24·5 and 45·4 respectively, and that the death rates per 1,000 live births in the first week after birth were 15·2 and 122·2 respectively. The excess mortality in twin pregnancy is mainly due to the greater incidence of very small babies amongst whom the death rate is high. Most of the deaths nowadays are of babies born so immature as to be incapable of independent existence. The main scope for lowering the mortality is to decrease the incidence of premature onset of labour, most of which is of "unexplained" aetiology.

The striking correlation between the height of the mother and foetal mortality suggests that one important reason for the excess mortality is the poor state of health, nutrition and physique of many mothers. It is possible that the increased growth of children reported to have occurred during and since the war (Boyne and Leitch, 1954) will decrease the differences in height and physique between the social classes and lead in time to a decrease in the prematurity rate in twin pregnancy. It might also lead to an increase in the incidence of twin pregnancy.

Possibly rest in bed during pregnancy would help to prevent premature labour, but if it were decided to give this method a serious trial, almost all cases of twin pregnancy would have to be admitted to hospital not later than the 32nd week of pregnancy since there is no way of selecting the women who are liable to have a premature labour. A practical difficulty would be that it is not always easy to diagnose twin pregnancy at the 32nd week.

To reduce the excess foetal mortality in twin pregnancy we should try to provide: (1) improved methods of treatment during pregnancy to prevent premature onset of labour, and (2) better circumstances during childhood and adolescence so that young women will be better developed and healthier and thus better able to carry a twin pregnancy to term without special treatment or having to spend a large part of the pregnancy in bed.

Summary

(1) A series of 397 twin pregnancies booked for delivery at Aberdeen Maternity Hospital over a period of 15 years is presented and the incidence of twinning is discussed.

(2) The foetal death rate is high and is due principally to prematurity.

(3) The neonatal death rate has fallen during the period of this survey. Part of this fall may have resulted from the war-time measures which helped to lower the overall stillbirth and neonatal mortality throughout Britain. Improved paediatric care has also been a factor.

(4) The method used to deliver the child at birth has much less effect on the mortality rate than has the size of the baby at birth.

(5) Twin pregnancy carries a high incidence of complications of pregnancy, especially pre-eclampsia, but the foetal mortality was as high or higher in the 47 per cent of pregnancies with no recognized complication.

(6) Rest in hospital antenatally appeared to help to prolong the pregnancy but this influence could not be measured accurately and may have been slight. Admission to hospital not later than the 32nd week would be necessary in all cases of twin pregnancy before the effect of rest in bed could be assessed accurately.

(7) A relationship was demonstrated between maternal height, the combined weights of the babies, and the foetal mortality rates. The lower mortality in tall than in small women appears to be due partly to their being less prone to premature onset of labour and partly to the greater vitality of the babies. The incidence of twinning appears to be greater in tall than in small women, and this observation, if confirmed by a large scale study, points to a correlation between the incidence of twinning and the state of nutrition of the mother, similar to that demonstrated in lower animals, especially the sheep.

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N-ALLYLNORMORPHINE IN THE TREATMENT OF NEONATAL ASPHYXIA

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IT is surprising that earlier and wider recognition has not been given to the possibilities of N-allylnormorphine in the prevention and treatment of neonatal asphyxia due to maternal sedation with drugs of the morphine, pethidine and amidone groups. This compound was first prepared by McCawley, Hart and Marsh (1941) and its effect in combating respiratory depression in animals was demonstrated by Unna (1943) and Hart and McCawley (1944) but little or no work was published on its effect on the human subject until Eckenhoff, Elder and King (1952), Adriani and Kerr (1953) and Fraser *et al.* (1952) demonstrated its effectiveness in cases of poisoning due to amidone, pethidine and morphine. Eckenhoff, Hoffman and Dripps (1952) were first to describe its use in the treatment of neonatal asphyxia and since then a further large series of cases has been published by Eckenhoff, Hoffman and Funderburg (1953) who found N-allylnormorphine effective when administered intravenously to the narcotized mother 10 to 20 minutes before delivery. These authors also describe a short series of cases in which the drug is given directly by the umbilical vein to the newborn infant and the value of this method of administration is emphasized by Chalmers and Thornberry (1954). In the present investigation a short series of cases treated by each of these methods is presented.

Methods GROUP 1

Data for the first part of the investigation were obtained from 100 uncomplicated confinements admitted to the wards of the Eastern District Hospital, Glasgow. Instrumental and operative deliveries were excluded from the series as it was considered that the administration of a general anaesthetic would make it more difficult to assess the value, if any, of N-allylnormorphine. For the same reason, cases in which the infant was under 5½ pounds in weight or cases in which there was evidence of foetal distress prior to delivery were also excluded from the series. All cases received either morphine or pethidine within 4 hours of delivery and the dosage of these drugs varied according to the requirements of the patient. No attempt was made to standardize dosage but in each case where morphine was administered the amount given was gr. ¼ of morphine sulphate and in no case did the quantity of pethidine given exceed 200 mg. In addition, nitrous oxide and air analgesia when required was administered by the Minnitt apparatus. Alternate cases received 10 mg. "Lethidrone" in 2 ml. saline administered intravenously by the antecubital vein and this injection was timed so far as possible to take place 10 to 20 minutes before delivery of the head. The time in seconds was carefully recorded for the infant to make its first gasp and thereafter to cry or to establish regular respiration. The muscle tone and colour of the skin as an indication of degree of oxygenation were also noted. After routine clearing of the air passages with the infant tilted head down, resuscitative measures were employed as indicated, oxygen administration by mask or nasal catheter,

artificial respiration by rocking and endotracheal intubation being resorted to at the discretion of the physician in charge of the case.

Results

Effect on the Mother of N-allylnormorphine

No untoward effects were noted in the mother and this is in accordance with the findings recorded by Eckenhoff *et al.* (1953). There was no evidence that the drug interfered with uterine action and no undue bleeding occurred during the third stage of labour in any of our cases. Eckenhoff *et al.* (1953) however report that in their series the majority of mothers who had opiates plus N-allylnormorphine required a weaker concentration of nitrous oxide than the control group. We did not find this to be so nor did we note, as they report, any marked degree of depression in the mother for 15 to 30 minutes after the administration of nitrous oxide but it is possible that we were using smaller concentrations of the gas.

Effect on the Infant

There were no infant deaths in the cases recorded. The overall figures for the series are presented in Table I and they indicate that

Table I

	N-allyl-normorphine	Control
No. of Patients	50	50
Average time to gasp (seconds)	18·4	28·1
Average time to establish respiration (seconds) ..	51·8	82·6
Required resuscitation ..	3 (6)	7 (14)

Percentages in brackets.

N-allylnormorphine is effective in reducing both the time taken for the infant to gasp and for the establishment of regular respiration. In addition it will be observed that in the N-allylnormorphine group there is a substantial reduction in the number of infants requiring active resuscitative measures. In all cases in which N-allylnormorphine had been administered to the mother prior to delivery the general condition of the infant at birth was excellent. Muscle tone was good and the heart sounds were regular and of good quality. Although active resuscitative measures were required in 2 cases, no great difficulty in establishing regular respiration was encountered. Table II and Table III allow comparison to be made between

Table II
Morphine Sedation

	N-allyl-normorphine	Control
No. of Patients	12	10
Average time to gasp (seconds)	24·5	36·6
Average time to establish respiration (seconds) ..	67·2	96·4
Required resuscitation ..	2 (16·7)	3 (30)

Percentages in brackets.

Table III
Pethidine Sedation

	N-allyl-normorphine	Control
No. of Patients	38	10
Average time to gasp (seconds)	16·5	25·9
Average time to establish respiration (seconds) ..	46·9	79·1
Required resuscitation ..	1 (2·6)	4 (10)

Percentages in brackets.

the cases in which morphine was given to the mother during labour and those in which pethidine was the drug of choice. It will be observed from these Tables that there was a more ready response from the infants in cases where pethidine was used. This is to be expected since the degree of respiratory depression is probably less here than in the morphine cases and this is reflected in the data for the control series.

Group 2

This group consists of 11 cases in which N-allylnormorphine was injected into the cord of the newborn infant. Three of these cases were to have been included in the control group for the foregoing series but, as the depressed condition of the infant at birth was a source of anxiety, it was decided not to withhold the drug. The dosage employed in all cases was 1 mg. in

2 ml. saline injected into the umbilical vein. In all cases, with the exception of one described below, a dramatic improvement occurred in the infant's condition. The 2 following case histories are illustrative.

Case 1

Mrs. M.J., a primigravida, aged 23 years, was delivered spontaneously after labour lasting 87 hours in the course of which morphine sulphate gr. ¼ was administered on 3 occasions, the last one being 63 minutes prior to the birth of the child. At birth the infant showed marked respiratory depression and made no attempt to breathe despite the usual resuscitative measures. Muscle tone was extremely poor and marked cyanosis was evident. Pulsation in the cord vessels was strong but slow (80 per minute). Lethidrone, 1 mg., in saline was introduced into the umbilical vein 4 minutes after delivery and was followed one minute later by the first spontaneous respiratory effort. Improvement in colour and in muscle tone followed rapidly and 4 minutes after injection the child was breathing regularly.

Case 2

Mrs. McD., aged 24 years, a primigravida, admitted in the 38th week of her pregnancy, was given a trial labour on account of pelvic contraction with disproportion. After 18 hours little progress had been made and as the foetal heart rate had fallen to 105 beats per minute and meconium staining of the liquor amnii was evident, Caesarean section was decided upon. Morphine sulphate, gr. ¼, had been given 1 hour 25 minutes previously. On delivery the child made no respiratory attempt and after 3 minutes, Lethidrone, 1 mg. in saline, was administered. Within 15 seconds respiration had commenced and in 2 minutes a lusty cry occurred to be followed by regular breathing with rapid improvement in colour and in muscle tone.

Case 3

This case failed to respond satisfactorily to N-allylnormorphine. Mrs. I.M., aged 34, primigravida, had been given Omnopon, gr. ½, as premedication for examination under anaesthesia (nitrous oxide, oxygen, ether) in the 36th week of a pregnancy which had been complicated during the previous 6 weeks by recurrent bouts of vaginal bleeding. Following examination, severe haemorrhage occurred due to partial separation of a centrally situated placenta praevia. Caesarean section was performed at once and a limp lethargic premature infant weighing 4 pounds 4 ounces was delivered. Lethidrone, 1 mg., was administered at once by the umbilical vein but no respiratory efforts occurred until 11 minutes after birth and regular respirations were not established for a further 12 minutes. It is considered in this case that, in addition to general anaesthesia, prematurity and ante-partum haemorrhage were factors contributing to the respiratory depression in the infant, and it was not therefore to be expected that N-allylnormorphine would provoke dramatic improvement.

Discussion

We agree with Eckenhoff *et al.* (1953) and with Chalmers and Thornberry (1954) that there is a definite place in obstetric practice for N-allylnormorphine in the treatment of neonatal asphyxia attributable to drugs of the morphine and pethidine groups.

At the present time the drug may be administered either to the mother before parturition or directly into the infant's umbilical vein after delivery and there is something to be said in favour of both methods. If given to the mother, it enters the foetal circulation *via* the placenta before delivery so that it has in theory at least a prophylactic action in the treatment of the infantile respiratory depression. This possible advantage is offset by the difficulty in assessing how much, if any, of the N-allylnormorphine has crossed the placental barrier. On the other hand if it is decided to withhold the drug until the child is born then an adequate dose can be delivered directly into the foetal circulation.

The data presented in Group 2 of this investigation indicate that a more profound infantile depression is to be expected in cases where morphia has been used in preference to pethidine. If it were reasonable to assume that a larger dose of N-allylnormorphine should be given to such cases then this larger dose could be given in part to the mother before delivery and, if need be, supplemented by a further dose to the infant after birth. This would help to counter the danger of overdose with N-allylnormorphine which appears to be in itself a depressant and the present method of administering an arbitrary dose of this preparation to all cases is not entirely satisfactory. Some attempt should be made to correlate dosage with the time of administration of the prenatal sedative and also its dosage.

At present the value of N-allylnormorphine is not that it permits of indiscriminate administration of morphine and pethidine to all parturients but rather that it allows these narcotics to be employed with greater confidence in cases where they are considered necessary—for example, severe pre-eclamptic toxaemia, prolonged labour with disordered uterine action, ante-partum haemorrhage and in cases where labour has progressed with

unexpected rapidity after the administration of a narcotic. N-allylnormorphine can also be used to counteract the depressant effects of opiates on the infant in cases where, due to the development of some obstetric complication, operative delivery becomes necessary in patients who are under the influence of these drugs. The deliberate use of opiates (covered by N-allylnormorphine) as premedication prior to operative delivery is not, however, justifiable as a routine procedure. In hysterical or over anxious patients the benefit of opiate sedation could be obtained without the depressant effects if N-allylnormorphine were administered to the mother at the commencement of the operation.

Finally it should be emphasized that N-allylnormorphine is only an adjuvant in the treatment of certain selected cases of infantile respiratory depressions and is not a substitute for the recognized methods of neonatal resuscitation which should be energetically employed in all cases where regular respiration is not satisfactorily established within a short time.

Summary

(1) A series of 100 deliveries occurring within 4 hours of the administration of opiate sedation to the mother is described. Fifty patients were given an intravenous injection of 10 mg. N-allylnormorphine 10–20 minutes prior to delivery. The remaining 50 patients served as controls. In addition, an injection of 0·2 mg. N-allylnormorphine was given into the umbilical vein of 11 infants delivered in a state of respiratory depression due to maternal opiate sedation. The condition of the child at birth and the intervals between delivery and establishment of respiration were noted.

(2) In cases in which N-allylnormorphine was administered to the mother there was a significant reduction in the interval between delivery and the establishment of respiratory efforts as compared with the control group. Injection of the drug into the umbilical vein of infants depressed as the result of uncontrolled opiate sedation produced dramatic improvement in all but one case.

(3) The advantages of different routes of administration of N-allylnormorphine and the optimum dosage and timing are discussed. The drug can be given with good effect to either mother or infant. On the whole administration to the mother by the intravenous route 10 minutes prior to delivery is preferred although the drug is likely to be effective if given at a shorter interval before delivery.

(4) The possible uses and applications of N-allylnormorphine in obstetrical practice are discussed.

(5) It is emphasized that the drug will merely counteract the effects of respiratory depression due to opiates. Foetal depression and anoxia may be produced by other factors operative in the same patient and active resuscitative measures are indicated if respiration is not established shortly after delivery.

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PERIPHERAL VASCULAR REACTIONS IN NORMAL SUBJECTS, NORMAL PREGNANCY AND TOXAEMIA OF PREGNANCY

BY

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THE vascular axon reflex in human skin has received considerable attention and many problems, related both directly and indirectly to this phenomenon, have been dealt with extensively. Lewis (1942) carried out a varied series of observations on one female patient with urticaria and drew certain conclusions about the postulated axon reflex and the nocifensor nerve hypothesis. Subsequently Lewis (1944) published a correction to some of the inferences drawn from these observations and pointed out the sex difference to the ionization of choline derivatives into the skin. With two adequate male and female groups he found that the normal females gave almost consistently positive results judged from the erythema and wheal formation whereas the male group, by comparison, gave almost uniformly negative results.

It appeared that the influence of oestrogenic or androgenic hormones played an important role in the type of skin response to histamine or H-like substances and to cholinergic compounds. In order to test this hypothesis and to determine if any new information might be gained, selected groups of subjects were submitted to the tests outlined. The correlation of test substances and the endocrine status of the subjects was the main object of the experiment, especially as it was possible to include patients with mild toxaemia of pregnancy according to the classification of Dieckmann (1952). The emphasis has been placed on the relationship of skin reactions to the response to a cholinergic substance and to histamine and the hormonal pattern of the subjects; these include normal subjects, treated normals and a varied selection of pregnancies. As it was a comparative study, it was decided to confine our attention to adrenal cortical steroids in the normal volunteers and to disregard A.C.T.H. The conditioning effects of adrenal steroids and of endogenous androgen secretion were of primary interest.

EXPERIMENTAL METHODS

Eight normal female and male volunteers were chosen from within the University. The pregnancy series consisted of 8 volunteer patients, in each group, from The King George V Memorial Hospital for Mothers and Babies. The pregnancy series received no pre-treatment and were tested by the ionization into the forearm skin of both carbachol (carbaminocholine chloride 0·1 per cent) and histamine acid phosphate (1/25,000). The normal subjects were tested similarly with each substance and again after 50 mg. tablets of cortisone acetate by mouth and 10 mg. of desoxycorticosterone acetate (D.O.C.A.) intramuscularly were given 48 and 24 hours before testing and after an appropriate interval had elapsed between the administration of the hormones. Subjects were tested in batches of four so that adequate control existed over the potency of the test substances and the Ringer's solution used as a control.

The method of testing was the use of apparatus fundamentally similar to that of Wayne (1933). The current density was of the nature of 20–40 microamperes, but it was maintained at about

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40 microamperes in the vast majority of cases. The areas of the skin erythematous responses were traced on to cellophane by grease pencil, transferred to ordinary paper and then measured by a planimeter. No account was taken of variability of skin resistance and some degree of uniformity was probably ensured by the careful washing of the test areas with ether.

Results

The results are presented in Tables I and II. There was not a sufficient number of positive reactions in the normal male groups and the late normal pregnancy group for the planimetric results to be treated statistically and these groups have been omitted from Table II.

Blood pressure measurements were made on each subject but there appeared to be no correlation between blood pressure level and the type of skin response so these observations have also been omitted. One presumably normal female was eliminated from that particular series because she had acne of the face and both the front and back of the chest; she fell into what may be termed the "androgenic category" in that she gave no positive responses whatsoever.

The total number of wheals associated with an erythematous response was 22 and 20 developed wheals after histamine and only 2 after carbachol electrophoresis.

Discussion

The general results of the normal male and female skin tests confirm the observations of Lewis (1944). However, this study was extended to include the effects of adrenal cortical hor-

Table I*
Types of Subjects and Number of Positive Reactions

Groups of Subjects	After Histamine	After Carbachol	Erythema +Wheals	Total Number of Tests	Total Number of Reactions
(*a*) Normal males	2	3			
(*b*) Normal after D.O.C.A.	nil	1	4	48	11
(*c*) Normal after cortisone	3	2			
(*a*) Normal females	7	7			
(*b*) Normal after D.O.C.A.	6	8	10	48	42
(*c*) Normal after cortisone	6	8			
Early normal pregnancy	5	6	4	16	11
Late normal pregnancy	2	3	2	16	5
Toxaemia of pregnancy	4	4	3	16	8

* 8 in each group.

Table II
*Planimetric Measurements of Erythematous Responses**

Types of Subjects	Number of Observations		After Histamine	After Carbachol
	Histamine	Carbachol		
Normal females	7	7	18·0±6·0	15·5± 5·0
Normal after D.O.C.A.	8	6	17·1±4·6	20·8±10·7
Normal after cortisone	8	6	20·8±6·1	11·5± 2·8
Early normal pregnancy	5	6	15·4±7·8	13·9± 5·7
Toxaemia of pregnancy	4	4	10·8±6·4	9·7± 8·6

* The results show the actual area in square centimetres and the standard deviation.

mones and different states of pregnancy on skin vascular reactions. Several striking features emerged from the results. One was the marked difference in responsiveness to both histamine and carbachol in the normal males and females, including the results of their pre-treatment with D.O.C.A. and cortisone. D.O.C.A. appeared to have an inhibitory effect on the development of reactions in males whereas there was not much variation in the female groups. Strangely, the early normal pregnancies tended to the female response pattern, the late normal pregnancies to the male pattern with the toxaemias of pregnancy occupying an intermediate position. There was but little difference in the occurrence of wheal formation.

Lewis (1942) suggested an axon reflex in relationship to these skin reactions. The possibility of this had been envisaged as early as 1879 by Ray and Graham Brown, who suggested that "there is a local mechanism independent of the centres in medulla and spinal cord by which the degree of dilatation of the vessels (capillaries) is varied in accordance with the requirements of the tissues". (Quoted from Fulton, 1955.)

This surmise was an early anticipation of the subsequent work of substantial elaboration by Elliott and Dale (Loewi, 1955). Dale and Dudley (1929) isolated acetylcholine from horses' spleen and it has since been isolated from other tissues. There is some evidence that histamine is liberated by certain nerves, but this has been disputed. However, the fact remains that cholinergic, adrenergic substances and possibly histamine are associated with the neuro-humoral mechanism of capillary reactions. Whether an axon reflex is involved in the skin responses is a difficult problem, but there does not seem to be much doubt about chemical transmission. If this is the case, then it appears that the reactions are conditioned by hormonal influences and it seems that adrenocortical hormones are largely implicated, predominantly those that have androgenic properties or those with such potential actions.

The significant sex difference and the discrepancy between the early and late normal pregnancy groups, support such a contention. Adrenocortical steroids of the nature of 11-hydroxyandrosterone or even 17-hydroxy-corticosteroids (Bayliss, Browne, Round and Steinbeck, 1955) which are excreted in large amounts in some virilizing syndromes might have such a conditioning effect on capillaries and their reactions to the substances tested on the skin. Again, progesterone which has been suggested as one precursor of adrenal steroid synthesis could be responsible for the near male patterns of reaction in the late pregnancy groups. If the pregnanediol excretion levels are taken as an index, the progesterone blood level would be at a maximum in the third trimester (Browne, Henry and Venning, 1939) and our late normal pregnancies were drawn from this period.

The role of the pituitary gland is somewhat obscure, but the release of adrenotrophic hormone acting on the adrenal cortex is a possible factor. The fact that flare responses to both carbachol and histamine, excepting the male group after D.O.C.A., were relatively uniform is curious. Lewis divided the flare reaction after a triple response of white reaction, red reaction and wheal formation. The one really significant difference between the two substances was the proportion of subjects who developed wheal formation and the vast majority of these occurred after histamine testing.

One other interesting feature was the occurrence of erythematous responses by the ionization into the skin of two entirely different and unrelated compounds under various hormonal conditions. The responses were relatively uniform within the particular groups. The only marked difference was in the incidence of wheal formation. Dieckmann (1952) stressed the fact that the arterial capillary pressure is within normal range in both normal and toxaemic pregnant patients, but the permeability probably varies greatly under humoral and hormonal influences. Dale (1933) postulated the transmission of nerve impulses, both augmentary and inhibitory under such conditions.

Summary

The results of ionization into the skin of histamine and carbachol in normal males and females and after pre-treatment with cortisone acetate and D.O.C.A. are described. Groups of early normal pregnancy, late normal pregnancy and toxaemias of pregnancy were tested. There was a marked sex difference in the number of

positive responses in the normals under all hormonal conditions and there was a difference between the early and late normal pregnancies with the toxaemias of pregnancy having an intermediate grading between these two groups.

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A NOTE ON THE SIGNIFICANCE OF ATTEMPTED ABORTION IN THE AETIOLOGY OF CONGENITAL ABNORMALITIES

BY

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ALTHOUGH numerous causes of congenital abnormalities have been suggested, little attention has been given to the possible significance of attempts to procure abortion. There are two reasons why this possibility deserves consideration: criminal abortion is comparatively common; and the methods used are frequently such that, if they do not succeed in terminating pregnancy, they may interfere with the foetus or its blood supply.

The proportion of pregnancies which end as a result of illegal interference is unknown, but was assessed very tentatively by the Biological and Medical Committee of the Royal Commission on Population as between 2 and 5 per cent. In the light of other evidence in the literature this is a conservative assessment. Published estimates of the incidence of abortion are between 12 per cent (Wiehl, 1938) and 44 per cent (Brunner, 1941), and such values do not as a rule take account of early losses which occur with little interruption of the cycle (Hertig and Rock, 1949). It is generally believed that the proportion of abortions which are induced is high; 40 per cent was the estimate made by the Inter-Departmental Committee on abortion.

Some information about methods used to procure abortion was provided by Parish (1935), who investigated 1,000 cases treated in a single hospital. Approximately half the patients (485) admitted having attempted to terminate the pregnancy, in some cases by taking drugs (111) or with the assistance of an abortionist (9), but in most cases (365) by introducing an instrument directly into the vagina or uterus. Even when allowance is made for the unrepresentative character of the patients admitted to hospital, there can be little doubt that the methods most frequently used are such that, if they do not result in abortion, they may interfere with the foetus or its blood supply. It is this conclusion which makes it worthwhile to examine the possible significance of attempted abortion in the aetiology of congenital abnormalities, particularly those abnormalities—such as anencephalus and mongolism—which are laid down at about the time when interference is most common.

A possible objection to this suggestion is that the incidence of the two conditions mentioned is raised in late birth ranks (anencephalus) and at high maternal ages (mongolism), whereas illegal interference is sometimes thought to occur most frequently in the first pregnancies of young and unmarried women. The last impression is not shared, however, by many experienced observers. Nor is it confirmed by Parish's data (1935): only 41 of the women who admitted interference were single, and the common reason for interference was not illegitimacy, but economic need. Since economic difficulties become greater as the number of children increases, a rise in the incidence of an abnormality at late birth ranks by no means excludes the possible significance of attempted abortion.

This note gives the results of interrogation of 40 mothers of anencephalics. Patients were confined in 7 hospitals, and were interviewed shortly after the birth. Information about marital status, contraceptive practice, and, finally, whether an attempt had been made to induce abortion, was recorded at the end of a

full obstetric history. While there must always be some doubt about the reliability of answers to questions about abortions, when interrogated in hospital by an obstetrician, patients usually speak freely, and it is believed that the information obtained is in general acceptable. This conclusion is also suggested by Parish's experience (1935) referred to above.

The sex ratio of the 40 malformations (31 female, 9 male) is approximately the same as in most reported series. In 27 anencephalus was the only abnormality; in the remaining 13 other malformations were also present. Illnesses during pregnancy were: influenza (3 cases); anaemia (3); severe hyperemesis (11). One patient had a thyroidectomy at the second month, and 3 had bleeding during the first trimester. In the absence of larger numbers and a control series no significance can be attached to these findings.

Of the 40 patients, 35 were married at conception, 4 married after conception, and 1 was single at the time of the birth. Seven patients stated that the pregnancy was unwanted, but only 1 had used contraceptives to prevent it. Two patients admitted that they had attempted to procure abortion: one by taking "female" pills during the second week after the first missed period, and the other by douching with dettol from a syringe between the 6th and 8th weeks of pregnancy. This incidence of attempted abortion (2 in 40) is certainly within the range of the estimate made by the Biological and Medical Committee of the Royal Commission on Population (2–5 per cent).

These findings appear to exclude attempted abortion as a significant cause of anencephalus.

Acknowledgments

We are indebted to the obstetricians who permitted us to interrogate their patients.

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THORACOPAGUS: REPORT OF A CASE DIAGNOSED PRIOR TO DELIVERY BY X-RAY EXAMINATION*

BY

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"THERE are reckoned up many causes of monsters; the first whereof is the glory of God, that his immense power may be manifested to those which are ignorant of it . . . Another cause is, that God may punish men's wickedness, or show signs of punishment at hand . . . The third cause is, an abundance of seed and overflowing matter . . . If, on the contrary, the seed be anything deficient in quantity, some or more members will be wanting, or more short and decrepit . . . The ancients have marked other causes of the generation of monsters . . . the force of imagination hath much power over the infant . . . Monsters are bred and caused by the straightness of the womb . . . by the ill placing of the mother in sitting, lying down or any other site of the body in the time of her being with child . . . By the injury of hereditary diseases, infants grow monstrous, for crooke-backt produce crooke-backt, lame produce lame, flat-nosed their like . . . Monsters are occasioned by the craft and subtlety of the Devil."†

Thus wrote Ambroise Paré in the sixteenth century with reference to the causes of monsters. According to Ballantyne in his fascinating book on *Ante-natal Pathology and Hygiene—The Embryo*, published exactly 50 years ago, the case about to be described would come under the general term of "polysomatous terata", a name roughly corresponding to the "monstrosities by excess or abundance" of the earlier writers.

CASE RECORD

(*E.M. 986*)

The patient, aged 28 years, paid her first visit to the antenatal clinic at the 9th week of pregnancy and thereafter attended at regular intervals. The obstetric history consisted of 1 previous pregnancy which continued until term but was complicated by pre-eclampsia. Labour was terminated after 15 hours by forceps delivery of a female child weighing 9 pounds 2 ounces. This child, at the age of 3 years, had recently been admitted to hospital for investigation of a tumour of the right kidney. This was subsequently reported to be a nephroblastoma from which the child died soon afterwards.

At the 28th week of pregnancy clinical findings, including excessive size of the uterus, suggested the diagnosis of multiple pregnancy. This was confirmed by an X-ray examination which revealed two foetuses, the forecoming presenting by the vertex and the aftercoming lying in the transverse. The only abnormality noted was definite extension of both foetal necks.

At the 31st week there was noted bilateral ankle and tibial oedema and the blood pressure was 136/100 mm. Hg and the haemoglobin 55 per cent. A foetal heart was recorded as having been heard. Admission was arranged for the following day.

Iron deficiency anaemia was treated by intravenous iron therapy.

At the 33rd week no foetal heart could be heard and a second X-ray examination was carried out. At this time the unusual position of the foetuses was noted, the thoraces being approximated and both necks showing considerable hyperextension (Fig. 1). Review of the earlier films showed a similar but less obvious relationship between the foetuses. The unchanged relationship between the foetuses strongly suggested the existence of thoracopagus. A third X-ray examination carried out a few days later showed no alteration whatsoever in the findings (Fig. 2).

At the 34th week the haemoglobin was 78 per cent, the blood pressure was 135/90 mm. Hg and the oedema had disappeared with bed rest. There was a moderate degree of hydramnios. At this time there developed the clinical features of acute bilateral pyelitis. Continuous vomiting and progressive dehydration necessitated intravenous therapy. Over the next few days there was marked increase in the hydramnios and the girth measurement was now 46½ inches. The blood pressure was now 170/100 mm. Hg. A further X-ray examination made at this time showed no alteration in the findings and the diagnosis of thoracopagus was highly probable (Fig. 3).

At the 35th week vomiting continued and there was considerable respiratory embarrassment from the size of

* Presented at the 500th Meeting of the Edinburgh Pathological Club on Wednesday, 8th December, 1954.

† Corner, George W. (1944): *Ourselves Unborn*. Yale University Press.

FIG. 2

FIG. 1

G.D.M.

FIG. 3

FIG. 4

FIG. 5

FIG. 6

the uterus. No typical foetal heart sounds could be detected but a single soft blowing souffle at a rate of 120 per minute could be heard and this suggested a common heart in living foetuses. With the onset of labour pains, a decision as to the method of delivery became an urgent necessity. The patient was ill with gross hydramnios, dehydration and hypertension. Although the foetuses were small and premature it was decided that, in the interests of the patient, it would be wiser to deliver by Caesarean section rather than subject a seriously ill patient to the hazards of a difficult vaginal delivery.

A classical Caesarean section was performed at the 35th week. The operation presented no difficulties and the conjoined twins were delivered intact through an adequate incision (Fig. 4). After birth a single heart beat could be detected and there was attempted respiration by both foetuses. The heart beat and spasmodic gasping ceased altogether after a few moments.

The patient made a rapid and complete recovery and has since come through a third pregnancy with the vaginal delivery of an apparently, and to date, normal child.

I am grateful to Dr. Helen Barrett of the Anatomy Department for the following brief description of the specimen:

The female conjoined twins are united ventrally in the thoracic and upper abdominal regions (Fig. 5). Attached to the lower margin of the fused parts is a single umbilical cord containing 3 vessels. Fusion is continued upwards as far as the suprasternal notch. Above and below the region of fusion the twins appear normal. A sternum lies to each lateral side of the median region of fusion. This sternum is of normal form and bears the attachments of the right ribs of one foetus on one side, and those of the left ribs of the other foetus on the other side. The liver is common to the foetuses, a single umbilical vein and falciform ligament being present. The diaphragm forms a continuous sheet above the liver. At this stage in the dissection the right lung of one foetus and the left lung of the other are visible. The right lung has three, and the left two lobes. The common heart lies between the lungs (Fig. 6).

Summary

(1) The details of a case of Thoracopagus are presented.

(2) The condition was diagnosed in the antenatal period as a result of repeated X-ray examination.

(3) The pregnancy was complicated by hydramnios, pyelitis and pre-eclampsia.

(4) Delivery was effected by Caesarean section.

MATERNAL BLOOD AND BREAST MILK ESTIMATION FOLLOWING THE ADMINISTRATION OF CHLORAL HYDRATE DURING THE PUERPERIUM

BY

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IN a previous study it has been proved that chloral hydrate when administered to pregnant women in labour is recovered from the maternal blood, foetal blood and amniotic fluid within 15 minutes (Bernstine, Meyer and Hayman, 1954). Evidence of chloral hydrate and its metabolites was still present in the maternal blood and the foetal blood after 10 hours, The present study was undertaken as a sequence to the former investigation of maternal and foetal blood levels, following the administration of chloral hydrate during labour.

The drug was administered rectally (chloral hydrate suppositories 1·33 g.) to 50 patients at the Jefferson Medical College Hospital, who were delivered by the house staff. These women were nursing their babies.

The ages of the patients studied ranged from 15 years to 37 years. There were 18 primiparae and 32 multiparae, the patient with the greatest number of births was a para–11. The types of delivery were as follows:

TABLE I

Type of Delivery

	Spontaneous	Low forceps	Breech extraction
Number of patients	46	2	2

The types of anaesthesia employed are shown in Table II.

As soon as lactation had begun, the drug was administered and samples of maternal blood and breast milk were taken. In most instances specimens were obtained on the third post-partum day.

TABLE II

Types of Anaesthesia

	Local infiltration or Pudendal Block 1 per cent Procaine	N_2O and Local	N_2O	Gas-oxygen ether	No anaesthesia
Number of Patients ..	22	6	1	2	19

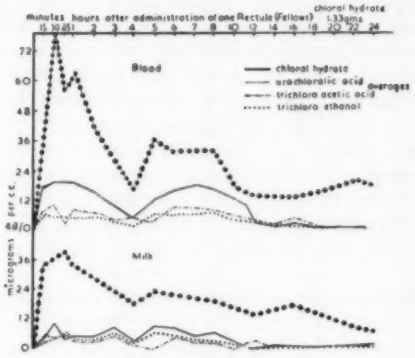
Procedure

The chloral hydrate suppository was inserted into the rectum (Quevauviller and Jund, 1951) by a nurse. The mother was advised that the suppository was not inserted to cause a bowel movement, but rather as a form of medication. After the proper time had elapsed, the breast was pumped using intermittent negative pressure of no greater than 7 mm. An arbitrary time limit of 10 minutes was used for obtaining the breast milk. Following this procedure the milk was transferred to a sterile container, using penicillin and sodium benzoate as preservatives. At this time 10 ml. of venous blood was withdrawn for similar estimation. No attempt was made to unduly hasten the flow of breast milk, and at no time did the patient feel more discomfort than if she were feeding her infant. If an inadequate amount of milk was obtained in the given time, the patient was not included in the study. No untoward effects were observed either in the mother or infant.

These specimens were examined quantitatively for chloral hydrate and its metabolites trichloroethanol, trichloroacetic acid and urochloralic acid. The time factor and its relation to the levels in the maternal blood and breast milk were observed. Samples of maternal blood and breast milk were taken for analysis from 15 minutes and at varying intervals up to 24 hours following the administration of the drug. The specimens were analyzed immediately after receipt in the laboratory. Four ml. of either milk or blood were necessary for analysis. (Table III.)

The chemical analysis was based on the reaction given by chloral hydrate compounds with pyridine and alkali, which permits colorimetric determination, as originally discovered by Fujiwari. Differentiation of the compounds was effected by the following method: the direct test gives chloral hydrate and trichloroacetic acid combined. Standing with alkali for 1 hour destroys the chloral hydrate so that a test performed after 1 hour yields trichloroacetic acid alone and thus the chloral hydrate is calculated by the difference. Trichloroethanol is extracted with pentane and thereafter oxidized with chromic acid to trichloroacetic acid and determined as such. For urochloralic acid an aliquot is evaporated and the residue is treated with chromic acid which transforms the urochloralic acid into trichloroacetic acid (Meyer and Smith, 1953).

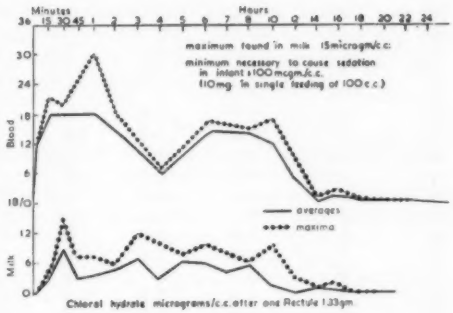
Following the examination of the first specimen which was taken 15 minutes following the administration of the suppository, evidence of chloral hydrate and its metabolites was evident quantitatively both in the maternal blood and milk. Graph I shows the averages of chloral hydrate, urochloralic acid, trichloroacetic acid


Minutes hours after administration of one Rectule (Fellows) chloral hydrate 1.33gms
15 30 45 1 2 3 4 5 6 7 8 10 12 14 16 18 20 22 24
Blood
chloral hydrate
urochloralic acid
trichloro acetic acid
trichloro ethanol
averages
micrograms per c.c.
Milk

Graph I

and trichloroethanol in maternal blood and milk. Of the 4 substances only chloral hydrate and trichloroethanol have hypnotic properties.

The observation obtained from the study of chloral hydrate alone is illustrated in Graph II


Minutes
Hours
15 30 45 1 2 3 4 5 6 7 8 10 12 14 16 18 20 22 24
maximum found in milk (5micrograms/c.c.
minimum necessary to cause sedation in infant (100 mcgm./c.c. (10mg. in single feeding of 100 c.c.)
Blood
averages
maxima
Milk
Chloral hydrate micrograms/c.c. after one Rectule 1.33gm

Graph II

which shows the average and maximum levels of chloral hydrate in blood and milk.

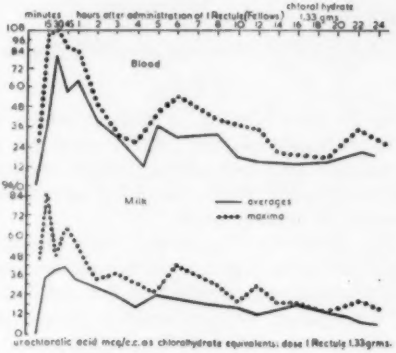
TABLE III

Expressed as mg./ml.

No.	Trichloroethanol		Trichloroacetic Acid		Chloral Hydrate		Urochloralic Acid		Time Hours	Mins.
	Maternal Blood	Milk	Maternal Blood	Milk	Maternal Blood	Milk	Maternal Blood	Milk		
1	2·0	+0	5·0	0	15·0	+0	0	0		15
2	2·0	1·0	0	0	21·0	+0	+0	+0		15
3	10·0	6·5	5·0	3·0	17·0	7·5	50·0	42·0		15
4	9·0	7·5	15·0	5·0	0	1·0	105·0	85·0		15
5	8·0	5·0	6·0	2·0	16·0	1·5	54·0	48·0		30
6	6·5	4·0	7·5	2·5	0	1·0	57·0	47·0		30
7	3·0	3·0	5·0	2·5	12·0	10·0	130·0	40·0		30
8	2·5	4·0	5·0	2·5	10·0	15·0	95·0	18·0		30
9	2·5	1·0	1·0	0	0	0	+0	+0		45
10	6·5	10·0	1·0	12·0	5·5	5·5	85·0	65·0		45
11	9·0	4·0	0	0	4·0	0	80·0	55·0		45
12	7·5	5·0	6·0	3·0	0	0	29·0	32·0	1	
13	4·5	5·0	7·5	2·5	7·5	2·5	62·0	52·0	1	
14	8·0	1·0	14·0	1·2	12·0	3·0	80·0	30·0	1	15
15	1·5	1·0	2·5	3·0	30·0	4·0	77·0	23·0	1	15
16	5·5	5·0	10·0	1·0	15·0	2·0	50·0	29·0	2	
17	5·0	4·5	6·0	+0	12·0	4·0	34·0	25·0	2	
18	3·5	4·5	5·0	2·0	17·0	4·0	30·0	33·0	2	
19	3·0	3·5	2·5	2·5	4·0	12·0	24·0	10·0	3	
20	6·0	6·0	4·0	2·5	7·5	4·0	29·0	22·0	3	
21	8·0	4·0	4·0	5·0	12·0	3·0	31·0	25·0	3	
22	4·5	4·5	7·5	2·5	10·0	4·0	32·0	37·0	3	
23	4·0	4·0	10·0	1·0	7·5	7·0	25·0	29·0	4	
24	1·0	1·0	5·0	1·0	2·5	2·5	15·0	9·0	4	
25	1·0	1·0	4·0	+0	2·5	0	6·0	20·0	4	
26	+0	1·0	0	+0	+0	0	10·0	10·0	4	30
27	14·0	5·0	5·0	+0	12·0	4·0	45·0	20·0	5	
28	4·0	3·0	2·5	+0	12·0	7·5	43·0	25·0	5	15
29	2·5	6·0	1·0	0	10·0	0	29·0	25·0	5	30
30	1·0	1·0	0	0	10·0	2·0	25·0	20·0	6	
31	5·0	2·0	4·0	0	12·0	6·0	56·0	40·0	6	
32	2·5	1·8	6·0	0	16·0	0	14·0	10·0	6	15
33	12·0	10·0	15·0	+0	17·0	9·0	30·0	19·0	6	30
34	6·0	4·0	12·0	5·0	15·0	1·0	43·0	30·0	7	
35	7·0	4·0	7·5	+0	15·0	1·5	12·0	90·0	8	
36	4·0	1·5	4·0	1·0	7·5	6·0	41·0	19·0	8	
37	3·0	1·5	5·0	1·0	7·5	5·0	20·0	9·0	9	
38	0	1·0	0	0	4·0	10·0	15·0	5·0	9	
39	2·0	1·0	6·0	0	10·0	4·0	14·0	15·0	9	30
40	6·5	2·0	7·5	+0	17·0	+0	32·0	20·0	10	
41	2·0	1·0	6·0	6·0	5·0	5·0	34·0	34·0	12	
42	1·0	1·0	+0	+0	+0	+0	0	0	12	
43	2·5	1·0	2·0	1·5	2·0	0	15·0	8·0	14	
44	+0	+0	0	0	0	+0	20·0	20·0	14	
45	0	7·0	15·0	0	2·0	0	10·0	15·0	16	
46	3·5	2·0	2·0	0	2·0	2·0	18·0	16·0	19	
47	+0	+0	+0	0	+0	+0	15·0	10·0	19	
48	2·5	1·0	1·0	+0	0	+0	20·0	20·0	21	
49	2·0	1·0	1·0	+0	+0	+0	3·5	3·5	21	
50	2·0	1·0	2·0	0	+0	+0	2·0	2·0	24	

+0=trace suppositories 1·33 g. given rectally.

In Graph III urochloralic acid shows a quick ascent in the blood and milk, then there is a decrease which is not as sharp as the rise. On specimens taken several hours later, there is a secondary rise which is not as sharp nor as high but the level is maintained for a longer time and the decline is more gradual.



GRAPH III

There is some parallelism between urochloralic acid and chloral hydrate absorption and excretion. At first there is a quick rise of urochloralic acid in the maternal blood and milk. At the same time there is also a rise of chloral hydrate in the maternal blood and milk, but this rise is not as sudden nor as great. Subsequently, there is a drop in the levels of both urochloralic acid and chloral hydrate. After a time there is an equivalent drop in the level of urochloralic acid in the maternal blood and milk. Throughout the entire period of time the level of urochloralic acid is maintained at a higher level than that of chloral hydrate. Trichloroacetic acid and trichloroethanol occur only in insignificant quantities, and consequently are not important in the interpretation of our findings. When levels of chloral hydrate in micrograms are estimated in the milk and evaluated quantitatively, the amount that the infant receives never exceeds 10 mg. of chloral hydrate/100 ml. of milk.

DISCUSSION

Fifty puerperal women who were nursing their babies were selected for this study. Chloral hydrate suppositories 1·33 g. were administered rectally to these patients. In a previous study it has been demonstrated that the rectal mode of administration gives more uniform levels than the oral, and moreover, these levels were attained rapidly. It was also found that according to studies when the suppositories are inserted not more than 5 cm. from the sphincter, the blood circulation does not drain into the portal system, but enters the general circulation. The specimens in most instances were obtained on the third post-partum day. Samples of maternal blood and breast milk were taken for analysis from 15 minutes and at varying intervals up to 24 hours, following the administration of the drug.

Evidence of chloral hydrate and its metabolites were found both in the maternal blood and breast milk within 15 minutes and up to 24 hours following the administration of the drug.

CONCLUSIONS

When chloral hydrate was administered rectally to nursing mothers (using 1·33 g. suppositories) evidence of chloral hydrate and its metabolites is found in both the maternal blood and milk. The levels found are parallel in the maternal blood and milk, but the levels in the milk are always lower. It may be stated that the administration of chloral hydrate in these cases did not affect the nursing infant adversely.

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GRANULOSA CELL TUMOUR PRODUCING SYMPTOMS FOUR YEARS FOLLOWING RADIUM MENOPAUSE

BY

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A NUMBER of cases in the literature are reported of oestrogenic tumours growing and causing symptoms after pelvic irradiation by radium or deep X-rays. Some writers have suggested that such irradiation might have a stimulating effect upon granulosa and theca cells. Traut and Butterworth (1937) record experimental work in mice, in which ovarian tumours have been produced by X-ray irradiation. Ingram and Novak (1951) mentioned 5 cases of feminizing tumour following previous pelvic irradiation. Douglas Matthews (1955) described 2 cases; first, a woman of 61 years, para-11, who had had an X-ray menopause for metropathia at the age of 53. This was followed by 6 months amenorrhoea, then 6 years irregular bleeding. At operation a thecoma was found with hyperplastic polypoidal endometrium. The second case described by Matthews was aged 58, para-5, who had a spontaneous menopause at 44 and thereafter irregular bleeding till 55–58. Following curettage a diagnosis of metropathia was made and this was treated by deep X-ray. Further bleeding occurred 3 years later and the findings were a granulosa cell tumour with polypoidal endometrium. It was thought likely that these tumours were in existence at the time of X-ray irradiation and continued to grow thereafter.

CASE REPORT

Mrs. M.B., aet. 50

This patient was admitted on the 8th March, 1954, complaining of two post-menopausal bleedings. The family history showed nothing relevant.

Previous history. The menarche was at 14. The periods were regular for many years—5 days every 28 days. She had 2 children which were born normally at term. There were no miscarriages. There had been no major operations and no medical illness requiring admission to hospital or nursing home.

The patient was quite well until December, 1948, when she began to have irregular, heavy, periods. She was admitted on 8th April, 1949, for a curettage, which revealed a simple endometrial polyp and a radium menopause was carried out, 100 mg. of radium being inserted for 24 hours. Following this the patient felt very well and put on much weight. In the spring of 1953 (4 years later) the patient had a slight loss of blood *per vaginam* for 2 days and this recurred in mid-February, 1954. There was no pain or any other symptoms associated with this loss of blood. The patient was not taking oestrogens. Her weight was going up slightly.

The patient's husband indicated that, during the previous 12 months, his wife had become much more irritable, also that during the last year her hair had become grey and she had aged.

An examination under anaesthesia was carried out on the 10th March, 1954 (4 years after the radium menopause); the uterus was larger than expected, the cavity measurement being 2½ inches. It was mobile but symmetrical and the right ovary was enlarged to about the size of a golf ball. Curettings were taken and a clinical diagnosis of a granulosa cell tumour was made. The report on the curettings showed: "Hyperoestrinaemia or possibly a very well differentiated adenocarcinoma."

On the 24th March, 1954, when the abdomen was opened, a firm tumour the size of a golf ball was found in the right ovary. A bilateral salpingo-oöphorectomy and total hysterectomy

FIG. 1

Endometrium showing marked Hyperplasia with Cystic Glands. ×20.

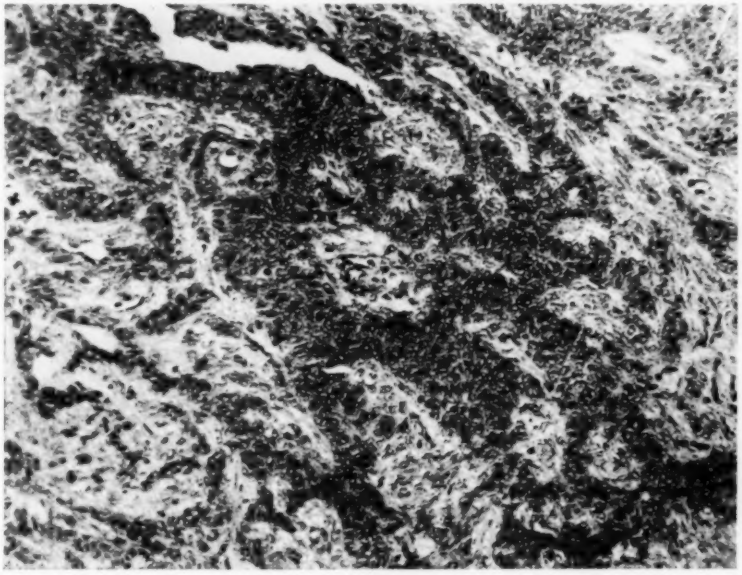

FIG. 2

Ovary showing Granulosa Cell Tumour. ×160.

were carried out. The report on the ovary showed a "granulosa cell tumour".

At the second follow-up on the 3rd January, 1955, the patient had no symptoms. The pelvis was clear, the vault scar was healed, there was no prolapse and she had no hot flushes.

The sections of the endometrium show a marked hyperplasia with cystic glands (Fig. 1). Some areas were very like an adenocarcinoma of the body, but three pathologists are quite clear that there is no question of malignant disease of the uterus.

The section of the ovary is typical of the cylindroma type of granulosa cell tumour which Novak considers must be labelled malignant (Fig. 2).

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A CASE OF CHORIOANGIOMA

BY

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IT is difficult to determine how rare the chorioangioma is. Marchetti (1939), in a valuable contribution to this subject, states that the tumour was found on 6 occasions in 20,000 successive deliveries at the New York Lying-In Hospital. As in the case of so many other rare conditions, the frequency with which the tumour is discovered is evidently determined by the vigilance exercised in its detection, especially as the tumour is often quite small and embedded in the substance of the placenta. Marchetti also quotes an earlier paper by Szarthmary (1934) who, as a result of what was evidently an exhaustive survey of the literature in 1934, collected 238 recorded cases. Like other uncommon conditions, no doubt a fair number of cases are observed from year to year but are not published.

The essential features of chorioangioma may be summarized as follows. It is a benign proliferation of capillaries derived from the placenta. It is somewhat controversial whether the condition should be regarded as a tumour or not. Dr. Stewart Smith, whose report on the pathology of this particular case is given later, has given me the following note which he considers represents the trend of present-day opinion. "While most pathologists accept that a true neoplastic angioma may exist, it is generally agreed that they are very uncommon and that most so-called angiomata are in fact angiomatoid malformations. This latter definition would undoubtedly apply to the placental lesion here described." For simplicity of expression the term "tumour" is used throughout this paper as it is almost invariably used in all others, even though its accuracy may still be *sub judice*.

As already mentioned, the tumour varies considerably in size. Marchetti mentions measurements varying from 0·5 cm. to 22 cm. in diameter, and the tumour may be solitary or multiple. The surface may be smooth, faceted or lobulated and the tumour is invested with a pseudocapsule composed of compressed and degenerated placental tissue. The tumour may be found anywhere in the placenta and is sometimes deeply buried, but the foetal or amniotic surface is the commonest site, while occasionally it may be found at the base of the cord. In some cases there are pedunculated outgrowths of the tumour. The tumour is typically of a deep purple colour and the cut surface resembles that of liver or spleen with fibrous trabeculae running through its substance. The more undifferentiated or cellular type is said to be paler in colour. As one would expect from a vascular and angiomatous tumour, it has a liberal blood supply through a leash of vessels derived from the placenta or the umbilical cord direct. According to Siddall (1924) this is the only direct connexion with the placenta in nearly half of the cases described. This is exemplified in the case shortly to be described where the vascular leash mimicked a second umbilical cord (Fig. 1).

The essential feature of the tumour when examined microscopically is the enormous number of capillary spaces containing red blood corpuscle, lined by only a single layer of endothelium with a variable amount of loose connective tissue between them. These are depicted in Fig. 2. The reader is also referred to the admirable camera lucida drawings in Marchetti's paper. In some cases, however, the cellular or more embryonic type of element predominates, giving rise to what has been described as a fibromatous or "sarcomatous" appearance, though even in these tumours irregular capillary spaces can be detected. The term "sarcomatous" applied to these tumours is

FIG. 1

Chorioangioma attached to placenta by short cord. Approx. $\times \frac{1}{4}$.

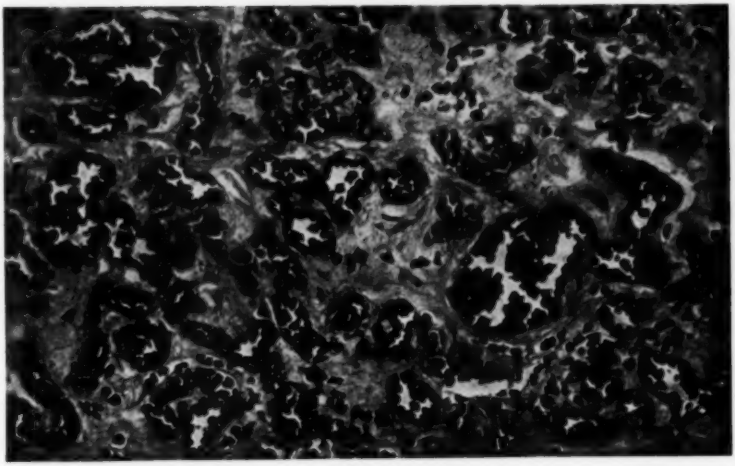

FIG. 2

Angiomatous spaces filled with blood. $\times 240$.

somewhat fanciful and based on their microscopical appearance.

In contrast to normal placental villi, where the capillaries are surrounded by cellular tissue and cytotrophoblast, this is absent, scanty or hardly recognizable in the chorioangioma and the capillaries are abundant and close together, forming the predominant element in the tumour.

There seems to be general agreement that this condition is never malignant. Both Marchetti's and Siddall's papers contain learned discussions as to the origin of these tumours and whether in fact they should be classed as tumours at all. Reference has already been made to this controversy. One can understand how difficult it must be to study the natural history of the condition, not only because it is rare, but also because of the fact that it is inaccessible and is in an organ, namely the placenta, which is itself only an ephemeral structure. It seems to be somewhat a matter of conjecture at what stage of pregnancy a chorioangioma begins to develop. It has also been observed in the bitch and the cow.

Chorioangiomata frequently have no effect on the course of labour or the development of the foetus, but hydramnios and prematurity evidently have some significant association with this condition and these in turn affect the stillbirth and neonatal death rate. The problem is discussed in great detail in Siddall's paper, to which the reader is referred and I cannot do better than quote his conclusion verbatim: "We are, therefore, led to the conclusion that the high foetal mortality concomitant with these tumours is largely a consequence of premature birth, the occurrence of which is increased as a result of the frequency of hydramnios." Horn (1948) has also described a case in which the presence of a chorioangioma simulated placenta praevia. On very rare occasions it has given rise to dystocia.

Case Report

Mrs. V.C., aged 36, and para-3, had a normal obstetric history. Her blood group was O Rh negative. No rhesus antibodies were demonstrable in the serum.

The present pregnancy was uneventful and the patient had a normal labour lasting about 4 hours. She was attended by a midwife.

The examination of the placenta disclosed the following appearance. At the margin of what was otherwise a normal placenta was a fair sized lobulated purple swelling. Not the least remarkable feature of this was the presence of a cord measuring approximately 5 cm. and about the size that one would associate with a 5-months foetus. In fact, at the time when confronted with this remarkable specimen and especially with what appeared to be 2 umbilical cords, I concluded erroneously that this must be a condition akin to foetus papyraceus and that the lobulated mass was what is described and depicted by Greenhill (1951) as "fetus acardiacus amorphus". The crux of the matter was whether the lobulated mass contained chorionic or foetal elements and it was decided to wait till the specimen had been photographed and hardened in formalin. After hardening, the cut surface of the mass looked not unlike liver or spleen, a resemblance which other writers have noted, and I am indebted to Dr. Stewart Smith for the following description of the pathology and photographs of the specimen.

Macroscopic. The specimen consists of a placenta 16 cm. in diameter to which the umbilical cord 50 cm. in length is attached, slightly eccentrically. The amnion and chorion are complete. Also arising eccentrically is a structure resembling an umbilical cord 5 cm. in length; it is coming from the placental surface and does not appear to have its own set of membranes. It is attached to a purple lobulated mass $10 \times 7 \times 5$ cm. which on section shows a smooth dark red surface and several large vessels.

Microscopical examination. Sections have been taken from the small flattened mass which was attached to the larger mass and appeared to be of similar nature. On the surface there are a few chorionic villi and a little syncytium. The rest of the material is composed of connective tissue of light texture in which are very large numbers of capillary vessels containing fresh blood. Some of these vessels are greatly dilated but most are quite small. Some ordinary arterioles are also present. The "cord" attached to the angioma consists of a single artery and vein not surrounded by Wharton's jelly.

The baby appeared normal and the puerperium was uneventful.

On the assumption that the baby might show some cardiac hypertrophy as a result of the vascular demands made by this large tumour, as is sometimes seen in uniovular twins or foetus papyraceus, it was seen by Dr. F. S. W. Brimblecombe a few weeks after birth and the size of the heart estimated radiologically and found to be normal.

Summary and Conclusions

A new case of chorioangioma is presented. The growth was distinct from the placenta and had attracted to itself a considerable vascular pedicle which by the time of delivery resembled an umbilical cord of about the twentieth week. This seems to throw some light on the problem of what stage in pregnancy this condition commences. In this case at least it strongly suggests that it originated in the first half of the pregnancy and probably at an early date.

As is not infrequently the case, no adverse effects were observed either on the mother, baby or the course of labour.

I would like to thank Dr. Keith Lockhart of Exeter, whose case this was, for his kind collaboration and Dr. G. Stewart Smith for his advice on the pathology of this condition and the photographs.

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ON THE STRENGTH OF THE FOETAL MEMBRANES

BY

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AND

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THE article by Dr. Mostyn P. Embrey "On the Strength of the Foetal Membranes" (*J. Obstet. Gynaec. Brit. Emp.* (1954), **61**, 793) has come to our attention. We are pleased to find that his conclusions are in general similar to our own (*Amer. J. Obstet. Gynec.* (1953), **65**, 480), but are distressed by his reference to the standard which we employed as "peculiar and mathematically incorrect". Because of this statement, we have subjected all of our data and calculations to the most careful scrutiny, and have been unable to find any errors in our reasoning or arithmetic, or to determine the factors which prompted the above criticism. In an effort to clarify Dr. Embrey's remarks and if need be to correct the impression which our article has given, it seemed desirable that the data be analyzed by a disinterested person whose work is primarily associated with the field of strain and stress, and whose opinion might be considered as authoritative. Accordingly, our original article, our data and calculations, and a copy of Dr. Embrey's article were sent to Dr. R. B. Banks, Associate Professor of Civil Engineering, Northwestern University, with the request that our method, our calculations, our data, and our conclusions be analyzed and, if possible, rationalized with the data reported by Dr. Embrey. Dr. Banks's analysis appears below.

REPORT BY DR. R. B. BANKS

I was requested by Dr. D. N. Danforth to review a paper which he and his colleagues, Dr. T. W. McElin and Dr. M. N. States, published recently entitled "Studies on Fetal Membranes" (*Amer. J. Obstet. Gynec.* (1953), **65**, 480). In addition, I was asked to criticize the experimental apparatus and technique which they employed in this study, to review the mathematical formula which they employed for computation and to calculate the results of a few of their experiments from their original laboratory data. This review was prompted by the article by Dr. Mostyn P. Embrey, "On the Strength of the Foetal Membranes" (*J. Obstet. Gynaec. Brit. Emp.* (1954), **61**, 793), in which data were published that were not in too close agreement with those presented in the former paper.

In the work of Danforth *et al.*, the "bursting tension", T, was computed from the well-known "spherical pressure vessel" equation, $T=PR/2$, in which P is the internal pressure and R is the radius of curvature. These factors, P and R, were correctly measured and the spherical shape of the stretched membrane justified the use of the above equation. Therefore, the values of the bursting tension, T, reported by these authors are numerically correct. Their T-values were computed and reported in the units of (cm. Hg)/cm., i.e., as obtained directly from the substitution of measured values of mercury column height and membrane radius. As is well known, a column of mercury H cm. in height exerts a pressure of (13·6) (H) g./cm.^{2} or (13·6) (980) (H) dynes/cm.^{2}. Thus, the conversion factor between the "bursting tension" values of the authors and the "tensile strength" values of Dr. Embrey is obvious. I am certain that Dr. Embrey will recognize that the units which the authors employed (viz., (cm. Hg)/cm.) are scarcely "peculiar" and certainly not "mathematically incorrect".

I was unable to discover the reason for the discrepancy between the mean T-value of 24 (cm. Hg)/cm. which the authors obtained and the 12·6 (cm. Hg)/cm. value which Dr. Embrey found. Naturally, one is first tempted to suspect that a factor of two was either neglected or introduced in computing the results of one or the other research study. After a careful review of the authors' paper and their basic data, I have concluded that the results which they reported are correct. I have also taken the liberty of reviewing the mathematical expressions of Dr. Embrey's paper. Although it may not be intuitively obvious, Dr. Embrey's tacit assumption that the shape of the deflected membrane is the segment of a sphere is correct. This can be shown by writing down the expressions for the equilibrium of an infinitesimal membrane area and applying calculus methods. Insufficient information was presented in his paper to allow one to compute a typical "tensile strength" value.

Assuming that the results which Dr. Embrey obtained do not reflect the omission of a factor of two, one can only speculate on the reason for the discrepancy between the two research studies. For example, the fact that Danforth *et al.* conducted their tests with the *chorion* exposed to the pressure whereas Embrey's tests were conducted with the *amnion* on the pressure side may be an explanation for the discrepancy. Future tests, with a ramification that an inert gas be used, would resolve this possibility. Speculating further, it may be possible that the dissimilarity of results may in fact reflect one of the "independent variables" which both research groups were seeking.

THE PREVENTION OF INHALED VOMIT DURING OBSTETRIC ANAESTHESIA

BY

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ONE of the most encouraging features of modern obstetrics has been the progressive decline in maternal mortality and morbidity. This is due partly to the progress in obstetric technique and facilities and partly to the introduction of ergometrine and antibiotics, together with the more general use of blood transfusion resulting in the better treatment of blood loss and sepsis. Regrettably, however, there are still many young women who lose their lives as the result of anaesthetics administered during their confinement. Approximately two-thirds of these deaths are due to the inhalation of vomit causing gross bronchial spasm and pulmonary oedema or overwhelming bronchial obstruction and pneumonic consolidation. Hence the incidence of anaesthetic deaths is assuming a relatively more prominent position in maternal mortality.

GASTRIC PHYSIOLOGY

During labour the stomach continues to secrete a gastric juice of high acid content and specimens of vomit collected at the end of the first stage of labour have shown a pH which varies between 1 and 2 (i.e. equivalent to $\frac{N}{10}$ – $\frac{N}{100}$ hydrochloric acid). Quite small quantities of this strongly acid fluid, if inhaled into the respiratory passages, will cause intense irritation of the lining mucosa and bronchial spasm.

In normal labour of relatively short duration the motility of the stomach is very considerably reduced and it is the common experience of every obstetrician to observe easily recognized foods in the vomit many hours after ingestion. This gastric atonia, which increases with the duration of labour, permits the accumulation of large quantities of partially digested food and volumes of up to 20 fluid ounces have been recovered as long as 10 hours after the administration by mouth of any fluids or solid food.

It is clear, therefore, that any attempt to ensure an empty stomach during labour can only be achieved at the expense of prolonged starvation and possibly prolonged intravenous therapy with its inherent dangers of electrolyte disturbance, but even this will not prevent the presence of a significant volume of resting juice with a high acid content.

EMERGENCY ANAESTHESIA

Many patients, however, require an anaesthetic soon after admission to hospital, when there will be no opportunity for a prolonged routine preparation. The necessity for general anaesthesia and the duration of labour cannot always be prophesied and food will often be taken in the presence of rapidly progressive labour.

There are also many obstetrical complications, such as foetal anoxia and retained placenta, which cannot be anticipated and which often demand immediate general anaesthesia. The consultant anaesthetist is rarely available for such emergencies and the relatively unskilled and inexperienced house officer is obliged to administer an anaesthetic to a completely unprepared patient.

The use of mechanical aspirators and the rapid assumption of the steep Trendelenburg position may lessen, but will not eliminate, the danger of inhaled vomit. The rapid induction of anaesthesia with intravenous Thiopentone may result in a silent regurgitation of gastric contents even before a relaxant can be injected and a cuffed intratracheal tube inserted.

Clinically it is impossible to assess the volume of gastric contents, but nevertheless for the safe induction of general anaesthesia the stomach

must be completely empty. The passage of a Ryle's stomach tube is always unpleasant and many patients will find it impossible. Aspiration often proves a lengthy procedure and, by reason of gross particulate matter and thick tenacious mucus, is frequently incomplete.

The recent investigation of 35 unselected patients at Guy's Hospital has shown that the administration of intravenous apomorphine hydrochloride is a very effective and safe pre-anaesthetic emetic.

Apomorphine Hydrochloride

Apomorphine hydrochloride is an artificial alkaloid prepared from morphine by dehydration. It is soluble in 60 parts of water and can be easily sterilized by boiling with 1 in 50,000 parts of phenyl mercuric nitrate. It acts as a strong emetic by stimulating the so-called vomiting centre of the medulla oblongata and produces intense nausea by stimulating the vagus. Its sedative and hypnotic effects are minimal and the drug is rapidly destroyed by the liver. On exposure to light it undergoes slow decomposition and any solutions which are emerald green in colour should be discarded.

Method of Administration

Ampoules of sterile apomorphine hydrochloride, gr. 1/20, were diluted with 10 ml. of sterile distilled water and after removing any dentures this solution was given by intravenous injection. Administration was continued slowly over 1 minute until the patient either complained of nausea or began to vomit. The amount required has varied between gr. 1/70 and gr. 1/30 although the average dose given has been gr. 1/45 which is approximately 1/6 of the usual hypodermic dose. After a short period of preliminary nausea the patient vomits profusely within 45 to 90 seconds of beginning the injection and this persists for a further 30 to 60 seconds. The feeling of nausea rapidly disappears as soon as the stomach is completely empty and within 3 minutes of the emesis. Atropine sulphate, gr. 1/50, is now given slowly by intravenous injection. This will rapidly antagonize the slight vagal effects of apomorphine and is also an essential premedication prior to general anaesthesia. The patient is instructed to clear her nasal passages and, after waiting a few minutes for the atrophine to take full effect, general anaesthesia is induced.

During the actual vomiting there is a slight increase in sweating and lachrymation and the pulse rate rises by 10 to 20 beats per minute. The blood pressure remains unchanged. Occasionally the patient has complained of slight vertigo, which has not persisted for more than a few minutes. No other side effects have been observed and the patient has been only slightly disturbed by the vomiting of very short duration.

It was thought that apomorphine might have a depressing effect upon the foetal respiratory centre. Six women have been delivered spontaneously, or by forceps under pudendal nerve block, after the administration of apomorphine, gr. 1/40, and in each of these cases the infant has cried vigorously immediately after birth.

It has been the custom to induce with oxygen, nitrous oxide and vinesthene and to maintain anaesthesia with ether. Many of these patients have retched during the post-anaesthetic recovery period when consciousness has almost been regained, but in 1 case only was this accompanied by vomiting of a few millilitres of fluid, which presumably had regurgitated through the pylorus during the anaesthetic. Provided the apomorphine is given within 15 minutes of the anaesthetic induction an empty stomach can be ensured and regurgitation of fluid from the small intestine need not be feared.

Conclusions

It is becoming generally recognized that low forceps and assisted breech deliveries can be easily and more safely effected under pudendal nerve block. On the other hand the more difficult forceps, breech extractions, internal versions and manual removal of placenta will in most cases require a general anaesthetic. It is hoped that the routine adoption of the simple technique described will effectively remove the greatest hazard in obstetric anaesthesia and will be acceptable to both obstetrician and anaesthetist.

Acknowledgment

I am indebted to Mr. J. B. Blaikley and to Mr. J. S. Tomkinson for permission to conduct this trial and my thanks are due to the Guy's Hospital Dispensary for the preparation of the ampoules of sterile apomorphine solution.

THE TUBAL MUCOSA IN ENDOMETRIAL CARCINOMA

BY

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AND

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FOR the past 5 years it has been the rule at the Women's Hospital, Liverpool, to examine a histological section of ovary, tube, endometrium and cervix in cases in which hysterectomy is carried out, irrespective of what other sections may be required for diagnosis. Even a cursory acquaintance with the material available shows that it confirms amply the well-accepted cycle in the mucosa of the tube and its correlation with the changes in the endometrium. It occurred to us that the material might be used also to cast light on another problem, viz., the relationship of hyperoestrinism to the development of carcinoma of the endometrium.

If persistent and prolonged hyperoestrinism were an important aetiological factor, it would be expected that in some cases it would persist after the development of the tumour, even though it might be more transient in others and have ceased before malignant change in the endometrium were discovered. In post-menopausal women with endometrial carcinoma a significantly raised number would show active tubal mucosa as compared with women without this tumour.

Material used. There were 50 endometrial carcinomas all proven by histology. They were not interviewed personally, but from their case sheets it appeared that 43 of them declared themselves to be past their menopause. Their age distribution is shown in the Table I. We are at a loss to explain the double peak in incidence. Seven women of the 50 declared that they were still having regular periods.

The control group consists of 43 consecutive women who underwent hysterectomy for non-malignant conditions, such as ovarian cysts and severe prolapse. Their age distribution is shown in Table I also.

In both groups the condition of the tubal mucosa was examined and placed in one of three groups. (*a*) Atrophic, flattened cells, which was, as expected, the most common post-menopausal condition. (*b*) As in the resting or early interval phase in the normally-menstruating woman. (*c*) Showing the tall columnar cells with crowding together and the production of "peg cells", as in the late interval phase of the normal cycle. No difficulty was experienced in classifying the mucosae according to this scheme. We have yet to see an atrophic tubal mucosa in a woman who is menstruating normally.

Results. The majority of the tubal mucosae in these post-menopausal women fell into the atrophic group but it was surprising to find that, while in the malignant group 33 did so, the condition was found in only 18 of the non-malignant cases. This leaves 10 of the women with endometrial carcinoma showing some tubal activity, but 25 of those without this cancer, an over-

TABLE I

Age	40–45	46–50	51–55	56–60	61–65	65–70	71–75	76–80
Endometrial Carcinomas	0	1	16	7	14	2	2	1
Other Conditions ..	1	7	12	11	4	6	2	0

whelmingly greater proportion. We consider this result to be convincing without statistical analysis.

Of the 10 cancer cases with active mucosae, 5 fell into our group (*b*) and 5 into group (*c*). Of the latter, i.e., those with more advanced changes, 3 fell into the youngest age group 51–55 years. Of the 25 active mucosae in the women without endometrial cancer, 17 showed early change, our group (*b*), and 8 more advanced development, our group (*c*).

Three of these 8 showed hypertrophy of the endometrium without malignant change, the only post-menopausal women in our series to do so. Indeed, even when cancer was present any unaffected endometrium found showed post-menopausal atrophy. Of the 3 with hypertrophy one was known to be taking oestrogens. In the second, however, no source of oestrogens could be discovered. A woman in the age group 61–65 years, she presented with post-menopausal bleeding and hysterectomy was performed. Apart from the hypertrophy of tubal mucosa and endometrium, the only abnormality found in the specimen was a small fibroma in one ovary. The third was probably not post-menopausal at all. She declared herself to be post-menopausal, so we included her in the series, but she had missed only two periods.

Summary and Conclusions

In 50 consecutive cases of endometrial carcinoma, 43 considered themselves to be post-menopausal. None showed hypertrophy of the unaffected endometrium, where it could be found, but 10 showed activity of the tubal mucosa.

In 43 control cases of post-menopausal women as many as 25 showed activity of the tubal mucosa and in 8 it was striking. Of these 8, 3 had concurrent endometrial activity. In 1 it was due to administered oestrogens, 1 was probably not past the menopause and in a third the cause was obscure.

These findings lend no support to the theory that hyperoestrinism may be a precursor of endometrial carcinoma. It appears that the tubal mucosa is a more sensitive index of the presence of circulating oestrogens than the endometrium.

Acknowledgments

We have to thank the Consultant Surgeons of The Women's Hospital, Liverpool for permission to use their cases.

SPONTANEOUS RUPTURE OF THE UTERUS DUE TO PLACENTA PERCRETA

BY

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IN the normal process of implantation of the ovum, the invasion of the trophoblast is limited by the response of the decidua. Wislocki, Dempsey and Fawcett (1948) have shown that the decidua contains a muco-polysaccharide by virtue of which the trophoblastic erosion is checked, the villi penetrating only as far as the spongy layer. It is through this layer that the placenta separates during the third stage of labour. Placenta accreta is the pathological condition in which this line of cleavage is absent—the villi being attached to the deep compact layer of the decidua in the case of placenta accreta vera and to the muscular layer of the uterine wall in the case of placenta increta, or have penetrated to the serosal coat in placenta percreta. Aaberg and Reid (1945) further subdivided these types into complete, partial or focal, according to whether the whole surface of the placenta, one or several cotyledons or only part of one cotyledon is adherent respectively.

The literature of spontaneous rupture of the uterus due to placenta percreta is here reviewed and a case report is presented of rupture due to partial placenta percreta.

INCIDENCE

Spontaneous rupture of the uterus due to placenta percreta is very rare. The case here presented is the only one that has occurred at Edgware General Hospital and Bushey Maternity Hospital, London in 40,249 deliveries between 1934 and 1954. No case has been recorded at Queen Charlotte's Hospital, London in 103,356 deliveries, between 1908 and 1954. Fitzgerald, Webster and Fields (1949) reported 1 case in 92,232 in Cook County Hospital, Illinois, between 1928 and 1948.

REVIEW OF THE LITERATURE

The first description that I have been able to find of spontaneous rupture of the uterus, proved microscopically to be due solely to placenta percreta, was published by Alexandroff in 1900, and since that time only 8 other cases have been reported (Bortkewitsch, 1911; Kratochvil, 1922; Dietrich, 1922; Bakanow, 1928; Pettit and Mitchell, 1949; Fitzgerald, Webster and Fields, 1949; McCarthy and Nichols, 1950; Schuyler, 1952). In addition, Krahulik (1952) and Lehmann (1925) each reported one case of spontaneous rupture of the uterus due to placenta percreta in congenitally abnormal uteri. Mr. Gibberd had under his care at Queen Charlotte's Hospital in 1948 a case of uterine rupture where the placenta had penetrated an old Caesarean scar, and a similar case was reported by Stone, Donnenfeld and Tanz (1954). These cases, however, are not included in the discussion, as the spontaneous rupture cannot be claimed as solely due to placenta percreta.

CASE REPORT

Mrs. E. Q., aged 43 years, was pregnant for the second time. Her first child was delivered in 1948 by lower segment Caesarean section after a trial of labour lasting 22 hours, because of uterine inertia and extended breech presentation. External cephalic version at 34 and 36 weeks had failed. The child weighed 7 pounds 6 ounces at birth and is alive and well. The temperature rose to 100·4° F. on the second and third day after operation, and at that time a heavy growth of *Bacterium coli* was obtained from vaginal swabs. A course of Sulphathiazole was given. The abdominal wound healed well. She was discharged from hospital with the child 14 days after delivery, and told that any future confinements should be in hospital.

On 10th January, 1953, the emergency obstetric service was called to her home by her doctor who had found her semi-conscious. Her last menstrual period had

been in August, 1952. She had been well until 2 days before, when she had complained of abdominal discomfort, with tenderness especially in the umbilical region. Four hours before her doctor had seen her she complained of colicky abdominal pain and a desire to defaecate. At stool she obtained some relief. A further attack of colicky abdominal pain occurred ½ hour later; it became more severe until finally 1½ hours later she had severe and continuous pain. She then complained of nausea and vomited twice. She complained of faintness and was noticed to be pale.

The doctor was called, but unfortunately could not be reached for an hour. He found the patient semi-conscious, extremely pale with a rapid feeble pulse and called the emergency obstetric service immediately.

When the obstetric service arrived the patient was cold, pale and restless. The radial pulse was hardly discernible and the blood pressure unrecordable. She groaned feebly when the abdomen was touched, but there was no guarding. The uterine outline could not be felt. There was no vaginal bleeding.

A diagnosis of intraperitoneal bleeding was made, morphia gr. 1/6 intramuscularly was given at once and a transfusion of one pint of Group O Rhesus negative blood was given in about 20 minutes. Little improvement resulted and a second pint of blood was given during transference to hospital. On reaching hospital an additional blood drip was started and endotracheal oxygen given. There was no improvement and death occurred 20 minutes after admission.

Post-mortem Findings

The peritoneal cavity contained 3 pints of blood. The uterus was of a size consistent with 20-weeks pregnancy. At the fundus was a large subperitoneal haematoma, diameter 5½ inches, in the centre of which was a perforation 3 inches in diameter through which placental tissue was protruding. The scar of the previous lower segment Caesarean operation was not identifiable. The uterus was opened anteriorly by a mid-line incision, and was found to contain a 20-weeks mature female foetus. The placenta was large, and symmetrically attached over the upper half of the uterus, with the cord arising centrally. At its lower edge the placenta was easily separated, but as the area of rupture was approached there was no apparent plane of cleavage. Histological examination of sections taken near the edge of the perforation showed in some areas no evidence of decidual tissue or myometrium, the chorionic villi having penetrated to the peritoneal coat. In other areas there was no decidual tissue and here the chorionic villi were seen to have invaded the myometrium, which showed hyaline degeneration. In some areas near the perforation a thin layer of decidua separated the villi from the myometrium.

The condition was therefore one of partial placenta percreta.

Discussion

All the cases that have been described of spontaneous rupture of the uterus due to placenta percreta have been multigravidae of widely differing ages, the youngest being 21 years (Fitzgerald, Webster and Fields, 1949), the oldest 43 years (the case here recorded) and except for these 2 cases the child was viable. No indication of the possible aetiological factor was given in 2 instances (Fitzgerald, Webster and Fields, 1949; Alexandroff, 1900) but in 8 cases there was a history of previous uterine sepsis or features, such as manual removal of the placenta or curettage, which were almost certainly accompanied by some degree of infection. In 2 cases (Dietrich, 1922; Bortkewitsch, 1911) no history was given of abnormal symptoms during the pregnancy, in 8 the presence of abdominal pain was recorded. Pettit and Mitchell (1949) and Schuyler (1952) record that their patients had menorrhagia prior to the pregnancy. No menstrual abnormality is recorded in the remaining 8 cases. Rupture occurred at the fundus uteri in 7 out of 10 cases, the exceptions being those of Bortkewitsch (1911), where the site was the posterior wall of the corpus, Bakanow (1928), the posterior wall of the lower segment, and Kratochvil (1922), who does not indicate the exact situation in the corpus. Five cases were complete placenta percreta and 5 partial, there being no apparent relationship of the degree of involvement to age, parity, stage of gestation, situation of the placenta or the aetiological factors concerned. In 2 instances, only, was the condition fatal to the mother, the case here described, who was moribund on admission to hospital, and that of Dietrich (1922) on whom vaginal hysterectomy was performed. The remaining 8 cases were treated by laparotomy, 7 by hysterectomy and 1 (McCarthy and Nichols, 1950) by local excision of the perfora-

tion and ligation of the Fallopian tubes with conservation of the uterus. In both fatal cases, however, there was some delay before treatment could be instituted. The child survived in 2 cases only (Bakanow, 1928; McCarthy and Nichols, 1950). In 8 cases the decidua was found microscopically to be either absent or deficient, in 2 (Fitzgerald, Webster and Fields, 1949; Schuyler, 1952) there was no mention of the decidua. Hyaline degeneration of the myometrium was noted in 4 cases (Dietrich, 1922; Bakanow, 1928; Schuyler, 1952; present report).

Conclusions

(1) Multiparity and intra-uterine sepsis, rather than trauma alone, are the main aetiological factors of placenta percreta.

(2) The depth of penetration of the chorionic villi and degree of involvement of the placenta depends neither on the age of the patient nor the stage of the pregnancy.

(3) Decidual deficiency is the basic lesion in all cases of placenta accreta.

(4) Abdominal pain during pregnancy associated with a history of uterine sepsis should raise in the obstetrician's mind the possibility of placenta accreta and hospitalization should be insisted upon.

I am grateful to Mr. E. ap I. Rosser, Senior Obstetrician and Gynaecologist, Edgware General Hospital, for permission to publish this case.

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A RARE CAUSE OF INTRA-UTERINE FOETAL DEATH

BY

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THE records of this case are presented to illustrate a rare cause of intra-uterine foetal death. External version under anaesthesia preceded foetal death, autopsy revealing a small intestinal volvulus. A short review of the literature and a comment follow the case report.

CASE REPORT

Mrs. Doris J., a primigravida aged 37 years, attended the antenatal clinic for the first time on 4th June, 1954. The date of the last menstrual period was 20th December, 1953 and the estimated date of delivery was 27th September, 1954. The patient gave a history of a chest injury sustained during nursing service in China during the second world war, but had had no other serious illnesses.

Physical examination revealed some scattered rhonci in the chest, but no other abnormality. *Blood examination:* Group "A": Rhesus negative to anti-D. No anti-Rh agglutinins were detected. Wassermann and Cardiolipin tests were negative.

The patient attended regularly for antenatal care and no abnormality was detected until the thirty-seventh week, when it was found that the foetus was presenting by the breech and external version in the clinic was not possible. The blood pressure at this visit was 140/90 mm. of mercury and it was decided to admit the patient and carry out external version when she was in hospital.

X-ray examination was carried out after the patient had been admitted to hospital and confirmed that the foetus was presenting by the breech, the legs being extended and the head badly flexed.

The blood pressure fell to normal within 24 hours of admission and external version was attempted the following day, without general anaesthesia, the patient being given Pethidine hydrochloride, 200 milligrammes intramuscularly, one hour beforehand. Despite good relaxation, version was not successful and version under anaesthesia was carried out 6 days later with nitrous oxide, oxygen, trilene and ether, the patient receiving atropine sulphate grain 1/100 and morphine sulphate grain 1/6 one hour beforehand. The foetal heart was heard prior to version and found to be at a rate of 110 per minute.

Version was successful but auscultation of the heart rate following the manœuvre revealed that this had fallen to 80 per minute. The heart rate remained at this level for the succeeding 10 minutes and then fell to 60 per minute. Immediate Caesarean section was contemplated, but, within 5 minutes, the foetal heart was no longer audible. There had been no external bleeding and the membranes had not ruptured.

The patient was returned to the ward after recovery from the anaesthetic and went into labour the following day, delivering herself of a fresh, stillborn, female infant. The membranes did not rupture until the time of full dilatation of the cervix and it was noted that there was no meconium staining of the liquor. The first stage of labour lasted 7 hours, the second 30 minutes and the third 5 minutes.

At the time of delivery, note was made that there were no knots in the umbilical cord, the cord was not wrapped around the foetus and examination of the placenta revealed no evidence of ante-partum separation.

The puerperium was uneventful and the patient was discharged 10 days after delivery, stilboestrol having been given in order to suppress lactation.

AUTOPSY REPORT

A well developed female child, 5 pounds 6 ounces in weight. The crown–rump length was 13 inches and the crown–heel length 19 inches. The head circumference was 12 inches. A large cephalhaematoma was present, but there was no intra-cranial injury.

On opening the abdomen, a greatly distended small intestine was immediately apparent and it was found that the mesentery of this was twisted anti-clockwise, thus producing early infarction of the mesentery and congestion and dilatation of the intestine, from a level of 4 cm. distal to the

FIG. 1

The photograph shows the grossly dilated small intestine, extending from a point 4 cm. distal to the duodenal termination to the ileo-caecal region. Thrombosis of the mesenteric vessels can be seen.

The normal sized large intestine is shown surrounding the dilated segment of the small intestine.

duodenal termination, to the ileo-caecal region (Fig. 1). The volvulus was easily untwisted.

Bile-stained fluid occupied the dilated intestine and the colon was entirely empty. The remaining findings included unexpanded lungs and an oedematous thymus gland, which was spotted with fine haemorrhages. No anatomical or morbid cause for the intestinal volvulus was found.

Discussion

Prophylactic external version has for long been practised as a method of management of the breech presentation, much discussion being centred around the question as to whether or not this should be carried out under general anaesthesia.

Amongst the hazards of the manœuvre listed by Hall (1953) is that of unexplained foetal deaths and this author reviewed those cases which had already been reported. Although some of the deaths remained unexplained, it was apparent that others were attributable to pre-eclamptic toxaemia and to rhesus incompatibility.

Vedder (1932) had one case of foetal death following external version, but the cause was not determined. Trubkowitch and Archangelsky (1944), in discussing the results of external version, were reticent as to the cause of death of the foetus which might follow the manœuvre. In fact, it has not been possible to find a similar case to the one described above in the literature.

Regarding the autopsy findings in the described case, it is difficult to conceive that external pressure on the foetus during version could result in volvulus of the small intestine. It is impossible to exonerate the manœuvre completely, however. One possible reason for unexplained foetal deaths following external version is that labour does not necessarily follow immediately, so that the foetus is born in a state of advanced maceration, making post-mortem examination valueless.

Acknowledgments

We would like to thank Mr. Humphrey Arthure and Professor W. St.C. Symmers for their permission to report this case and to Miss P. Turnbull for the photograph.

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A CASE OF PREGNANCY FOLLOWING BILATERAL ADRENALECTOMY FOR CUSHING'S SYNDROME

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PREGNANCY associated with Cushing's syndrome is a rare event, as this condition is typically associated with amenorrhoea, anovulation and infertility. Nevertheless Hunt and McConahey (1953) have collected 4 cases with a total of 7 pregnancies in the presence of active untreated Cushing's syndrome.

With recent advances in the surgical treatment of Cushing's syndrome, and the associated use of cortisone, it seems likely that pregnancy under these circumstances will become more frequent. Hunt and McConahey (1953) also described 5 cases of pregnancy after treatment of Cushing's syndrome. Four of these cases had been treated by adrenalectomy, and one by deep X-ray therapy to the pituitary gland. In 4 of their cases, the pregnancies went to term, and the deliveries were normal. Two of these were multiparae, and in the other 2 the parity was not stated, although one was presumably a primipara. None of these was having replacement hormone therapy. The fifth patient showed evidence of adrenal cortical insufficiency, and, despite treatment with cortisone and desoxycorticosterone acetate, the pregnancy terminated in spontaneous abortion at 2 months.

CASE REPORT

Mrs. J.H., aged 32 years, attended one of us (K.G.W.) on 6th August, 1954, stating that her last normal menstrual period commenced on the 11th June, 1954. A Hogben test for pregnancy had been carried out on 2nd August, and was found to be positive. On vaginal examination her uterus was found to be enlarged to the size of a 6-weeks gestation, and the expected date of confinement was estimated as being 18th March, 1955.

Her past history was as follows: At the age of 17 years, she developed the manifestations of Cushing's syndrome. She started to menstruate at this time, but her menses ceased again after 3 months. She put on weight rapidly and became lethargic and flushed. Nine years later she attended the Alfred Hospital, Melbourne, and appeared to have a fully developed Cushing's syndrome, with typical buffalo obesity, hirsutism of her upper lip, plethoric moon face, poor wound healing powers, and amenorrhoea. Her blood pressure was 180 millimetres of mercury systolic, and 110 millimetres diastolic, and she weighed 224 pounds. She also had glycosuria, a diabetic glucose tolerance curve, and a high corticoid excretion in her urine.

Unilateral adrenalectomy was performed in 1950, and she improved, but the picture of Cushing's syndrome gradually returned. Deep X-ray therapy to her pituitary gland, and injections of testosterone propionate did not produce any substantial improvement, so her remaining adrenal gland was removed *in toto*, and, after maceration, a portion was transplanted into her thigh. Evidence suggested that the graft had taken in its new position, and was her only viable adrenal tissue. About 10 months later, this area was subjected to deep X-ray therapy, as the features of Cushing's syndrome reappeared, although they had disappeared earlier. They again gradually disappeared and her condition improved.

Complete physical and endocrine examination revealed a fairly normal woman. She did however complain of tiredness, and her haemoglobin would fall to about 70 per cent every 2 to 3 months. She was given occasional blood transfusions, as she could not tolerate iron by mouth, and intravenous iron therapy became a formidable procedure as her veins were very poor.

Supportive endocrine therapy was given in the form of 25 to 50 milligrammes of cortisone orally per week in divided doses. She improved with this, and it was decided that she was maintaining a reasonable state of endocrine balance. She commenced to menstruate regularly, but suffered considerable dysmenorrhoea.

Basal temperature charts indicated that she was ovulating, and she was advised that she could become pregnant.

During all of the above, she was found to be very sensitive to minor stress and to operations, and it was thought advisable to give desoxycorticosterone acetate and cortisone prior to any operative procedure. This was done before two minor procedures—removal of a panniculus abdominis, and incision of a perianal abscess. In both of these operations, and also during the major operative procedures, she developed a state of severe circulatory collapse, despite adequate pre-operative and post-operative supportive hormone therapy. Her pulse rate would rise to about 180 beats per minute, and systolic blood pressure would fall to about 70 millimetres of mercury. This was thought to have been related to loss of adrenal medullary tissue, and the use of nor-adrenaline was recommended in any operative procedures, or those associated with pregnancy and labour.

She married early in 1954, and came to live in Perth. On 1st June, 1954 she was admitted to the Royal Perth Hospital for a blood transfusion. She was then 5 feet tall and weighed 126 pounds. She still had some girdle distribution of fat, and a fine pigmentation was noted on her shoulders. Her blood pressure was 140 millimetres of mercury systolic, and 90 millimetres diastolic.

The following investigations were carried out at this time:

Urinary neutral 17-ketosteroids—0·3 milligrammes per 24 hour volume of urine (585 volume millilitres per 24 hours).

Serum phosphorus—4·3 milligrammes per 100 millilitres.

Serum sodium—137 milli-equivalents per litre.

Serum potassium—4·1 milli-equivalents per litre.

Serum chlorides—110 milli-equivalents per litre.

Carbon dioxide combining capacity—21·5.

At this time she was menstruating for 2 to 3 days every 28 days. She then missed an expected period in July, and came into our care.

Her condition remained satisfactory throughout pregnancy, until 21st February, 1955, when she was admitted to hospital. Her weight had increased to 149 pounds and the maximum blood pressure recorded on admission was 138 millimetres of mercury systolic, and 88 millimetres diastolic. Her haemoglobin had fallen from 12·7 grammes per 100 millilitres to 9·3 grammes, so she was given a blood transfusion of 2 pints of packed red cells. She was at this time receiving 12·5 milligrammes of cortisone daily.

Her whole condition was reviewed at this time, and, in view of her previous history of collapsing under anaesthesia or at times of stress, it was decided that it would be safer to deliver her by Caesarean section, with controlled anaesthesia, rather than subject her to the unpredictable risks of labour, which could be prolonged and perhaps difficult, although there was no actual obstetrical contra-indication.

Lower uterine segment Caesarean section was performed on 5th March, 1955, when her pregnancy had advanced to 38 weeks—clinically and according to her dates.

Pre-operative medication consisted of four doses, each of 50 milligrammes of cortisone, at 6-hourly intervals, and 1 hour beforehand she was given 20 millilitres of Eschatin (P.D.) (adrenal cortical extract), by intramuscular injection. An intravenous drip of 5 per cent dextrose solution was also commenced.

Thiopentone, 0·3 grammes, were given intravenously for induction of anaesthesia, and a further maintenance dose of 0·1 gramme was required during the operation. A total of 400 milligrammes of Scoline was given intravenously for endotracheal intubation and maintenance of relaxation. Nitrous oxide and oxygen anaesthesia in the ratio of 2 to 1 was used throughout. Pethidine, 100 milligrammes, was given by intramuscular injection at the time of the birth of the baby, which cried upon the table, but was subsequently apnoeic and was resuscitated by intragastric oxygen and rocking for 6 minutes, before establishing rhythmical respirations.

Throughout the operation, the patient's blood pressure remained constantly at 170 millimetres of mercury systolic, and 110 millimetres diastolic, but her pulse rate rose to 160 beats per minute. She became conscious shortly after the abdominal incision was repaired and her condition remained satisfactory.

Three hours after she was transferred to the ward her blood pressure had fallen to 108 millimetres of mercury systolic, and 64 millimetres diastolic, but her pulse rate was only 104 per minute. So nor-adrenaline (2 millilitres per pint) was introduced into the intravenous drip. This was discontinued after 3 hours, following which her blood pressure remained fairly constantly at the level of 124 millimetres of mercury systolic, and 8 millimetres diastolic, whilst her pulse rate varied from 96 to 112 per minute. The intravenous drip was removed 21 hours after the operation.

Thereafter her puerperium was quite uneventful. She sat out of bed on the fourth day, and was discharged on the fourteenth day, by which time the dosage of cortisone had been gradually reduced to 25 milligrammes daily. At the time of discharge per pulse rate was still rapid—96 beats per minute, whilst her blood pressure varied from 120 to 130 millimetres of mercury systolic, and 68 to 92 millimetres diastolic.

A urinary neutral 17-ketosteroid excretion estimation, carried out on the third day of the puerperium, was 3·3 milligrammes in 24 hours, whilst the excretion of a normal puerperal patient used as a control was 6·6 milligrammes.

The baby weighed 6 pounds 8 ounces at birth, and it was observed that her anterior fontanelle was almost completely closed. Subsequent radiological investigation showed no evidence of abnormal ossification. On the advice of a physician the baby was artificially fed, and left hospital with the mother, on 19th March, 1955, thriving and weighing 6 pounds 7 ounces.

At postnatal examination on 9th May, 1955 the patient was feeling and looking well. The abdominal scar was well healed and the uterus involuted. Her blood pressure was 140 millimetres of mercury systolic, 80 millimetres diastolic. The baby was thriving and weighed 8 pounds 4 ounces.

Comment

Despite the number of cases of this nature collected by Hunt and McConahey (1953), this must still be considered a rarity.

Caesarean section was performed for medical indications, and was considered to be justifiable, in view of the unpredictable outcome of labour in a primigravida with a history of poor response to stresses. It was thought that the larger doses of cortisone administered pre-operatively prevented the occurrence of shock during the operation in this case. Incipient shock during the initial post-operative period was overcome by the intravenous administration of nor-adrenaline.

Collapse in response to stress or operative procedures in these cases is similar to that obtaining in Addison's disease, and appears to be due to a deficiency of functioning adrenal medullary tissue. Pregnancy in Addison's disease was described and reviewed by Rolland *et al.* (1953).

An interesting comment made by Hunt and McConahey (1953) is that undiagnosed adrenal deficiency may cause "obstetric shock" and maternal death following delivery. This is likely to occur in cases where function of the adrenal glands has been suppressed by the recent administration of cortisone. They state that patients with adrenal cortical insufficiency usually do well during pregnancy without treatment of this insufficiency.

Summary

A pregnancy in a patient, who had undergone bilateral adrenalectomy for Cushing's syndrome, is described. Cortisone was administered during pregnancy and the patient was delivered by Caesarean section.

Recovery was uneventful, and the patient's hormonal balance seemed to be improved by the pregnancy. The baby did not appear to be affected in any way.

Reference is made to the literature concerning the treatment of similar cases.

We are indebted to Dr. Sam Rose of Melbourne for the notes concerning this patient's early history. We wish to thank Dr. J. Calder and Dr. A. E. Hocking for assistance in regard to the medical treatment and anaesthesia in this case.

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AN INVESTIGATION OF THE GROWTH OF THE FOETAL SKULL IN THE LAST FOUR WEEKS OF PREGNANCY BY RADIOLOGICAL CEPHALOMETRY

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INTRODUCTION

IN 1929 Scammon and Calkins made the statement that the foetal biparietal diameter increases by approximately 2·5 mm. per week. In the next few years many methods of radiological cephalometry were described and Reece (1935) confirmed the figure previously given by Scammon and Calkins.

Moir (1943) stated that the biparietal diameter probably increased by 1–1·5 mm. per week in the last month of gestation but 3 years later (Moir, 1946) he stated that in estimating the possibility of difficult labour he allowed for a growth of 2 mm. per week in the biparietal diameter.

Josephs (1949), using a new method of cephalometry which he did not describe, measured the biparietal diameter of 189 cases during the last weeks of pregnancy and again by direct measurement with callipers 3 days after birth when moulding had disappeared. He came to the rather surprising conclusion that there was no sign of a growth curve between the 36th and 40th weeks of pregnancy.

Macdonald (1952) measured clinically the biparietal diameters of 1,059 newborn infants and plotted these in a scatter graph against the estimated duration of pregnancy. He deduced that the average biparietal diameter increased in size by 4 mm. during the last 4 weeks of pregnancy. Crichton (1952) measured *in utero* the biparietal diameter in 68 cases after the 36th week of pregnancy and those babies delivered not less than a fortnight later were subjected to radiological cephalometry 72 hours after birth. He concluded that the biparietal diameter increased by 1–1·2 mm. per week during the last weeks of pregnancy.

THE INVESTIGATION

In 1950 when a new department of Radiology was opened in the Royal Maternity Hospital, Belfast, it was decided to use the method of pelvimetry described by Moir (1946). It was noted in the erect lateral view that in a high percentage of cases the foetal skull engaged in the pelvis with the occiput lying transversely so enabling the biparietal diameter of the foetal skull to be measured.

It was arranged that all primigravidae attending the antenatal clinic should be referred to the X-ray department at approximately the estimated 35th week of gestation. An erect lateral view of the pelvis was taken and if the occiput was transverse the patient had a repeat erect lateral radiograph taken weekly until labour started.

A high percentage of cases were suitable for follow-up at the initial examination but unfortunately rotation from the transverse position frequently occurred until the head engaged so that one often found the head lying transversely at the 36th week, obliquely at the 37th week and again transversely at subsequent examinations.

By following up 493 patients it was possible to collect 100 cases where the foetal skull remained in the transverse position from 36 weeks until labour started.

As a check on the radiographic measurements of the foetal skull *in utero* the babies' skulls were measured personally with engineer's callipers within 24 hours after birth and also

TABLE I

Increase in Biparietal Diameter in Millimetres	Number of Cases			
	During 4th Week Before Delivery	During 3rd Week Before Delivery	During 2nd Week Before Delivery	During Week Before Delivery
−2 mm.	0	0	1*	0
−1 mm.	0	0	0	0
0	11	12	18	9
+1 mm.	47	50	42	45
+2 mm.	21	19	12	22
+3 mm.	0	0	0	0
+4 mm.	1	0	0	0
Total number of cases	80	81	73	76
Average increase in biparietal diameter per week	1·16 mm.	1·09 mm.	0·88 mm.	1·17 mm.

* Moulding.

3 days later whenever moulding was assumed to have disappeared.

It was obviously impossible to arrange for patients to be X-rayed at exactly 4 or 5 weeks before confinement and therefore growth in the 4th week before delivery was measured by subtracting the biparietal diameter measured on a radiograph taken between 4 and 5 weeks before delivery from the measurement on a radiograph taken between 3 and 4 weeks before delivery. Similarly the growth was measured for the remaining 3 weeks before delivery.

RESULTS

The weekly increase in the biparietal diameter for the series of cases is recorded in Table I.

It will be noted that figures for the growth of the complete 100 cases are not given for each week. The omissions of some of the cases were due to one of two reasons: (*a*) Patient missed a visit to the antenatal clinic and thus an erect lateral view of the pelvis was not taken; (*b*) Slight rotation of the foetal skull occasionally occurred and an accurate biparietal reading could not be obtained.

No case however has been included in the series if less than 3 weekly readings were obtained.

The figures show that during the last 4 weeks of pregnancy the biparietal diameter of the foetal skull increases by approximately 4 mm. and this increase is a gradual one taking place over the entire 4 weeks and averaging 1 mm. per week.

It was noted that the biparietal diameters varied between 8·1 cm. and 9·9 cm. 4 weeks before birth and between 8·6 and 10·2 cm. 3 days after birth. The increase in the biparietal diameter did not appear to vary with the size of the foetal skull.

These figures confirm the accuracy of Macdonald's (1952) deductions and they also confirm the figures given by Crichton (1952) whose cases were only measured on one occasion *in utero* whereas in this series the cases were measured weekly *in utero* by radiological cephalometry.

SUMMARY

The biparietal diameters of 100 foetal skulls have been measured weekly by radiological cephalometry during the last 4 weeks of pregnancy and show an increase of approximately 1 mm. per week during this period.

ACKNOWLEDGMENTS

I should like to thank Dr. W. H. T. Shepherd for his helpfulness and advice and also the Medical Staff of the Royal Maternity Hospital for allowing me to investigate their patients.

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A NOTE ON THE ORIGIN OF THE PSEUDOMUCINOUS CYSTADENOMA OF THE OVARY

BY

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DESPITE recent work on the histogenesis of ovarian tumours, the origin of the pseudomucinous cystadenoma still remains in doubt. Several theories have been advanced in explanation and, according to Willis (1953), three of these are that it arises by unilateral development of a teratoma, that it is related to the Brenner tumour or that it is related to the serous cystadenoma, the epithelium undergoing a metaplastic change. The first of these theories was especially favoured by Meyer and Ribbert (cited by Novak, 1952) although Meyer considered that a certain small proportion of these tumours had their origin in Brenner tumours, and it has remained probably the most widely held view on the matter. On this account, it is felt that publication of the findings in a very early pseudomucinous cystadenoma may be of interest, as they appear to show a definite origin for the tumour in the germinal epithelium of the ovary.

The patient was a woman aged 43, who had a total hysterectomy performed, including removal of both appendages. The left ovary contained a typical pseudomucinous cystadenoma about 7 cm. in diameter; the right ovary appeared normal, but on gross section a tiny mucus-containing cyst was noted. A single routine section showed a very early pseudomucinous cystadenoma consisting of a small cyst cavity with a few smaller loculi lined by the characteristic epithelium between it and the surface of the ovary and which appeared to be arising from the germinal epithelium. Multiple sections were then cut through the ovary and stained with haematoxylin and eosin and by the periodic acid-Schiff technique with the following results.

As can be seen by reference to Fig. 1, the germinal epithelium on the surface of the ovary on one side of the localized area of origin begins to get taller and rather papillary, and then in the haematoxylin and eosin stained sections there can be observed the appearance of bluish "mucoid" material which gradually increases in amount and becomes clearer until the epithelium is the typical tall, columnar, pale-staining type that is seen in the pseudomucinous cystadenoma. At the other side of the site of origin (Fig. 2) the transition from cubical "germinal" to columnar "pseudomucinous" epithelium is quite abrupt. Between these, there are many clefts on the surface of the ovary lined by "pseudomucinous" epithelium (Fig. 5), and some of these can be seen to be cut off from the surface, with the formation of a very early cystadenoma (Fig. 6). As the "germinal" epithelium is seen to be quite continuous with the "pseudomucinous" epithelium, with a transitional zone in one area, it is felt that this case provides at least some evidence in favour of the view that the pseudomucinous cystadenoma arises by metaplasia of the germinal epithelium of the ovary in a manner similar to the serous cystadenoma.

This proposition means that some apparent anomalies of behaviour of certain ovarian tumours can now be explained. The occurrence of cystadenomas containing both serous and pseudomucinous epithelial elements is well-recognized, and this is easily understood if both arise by metaplasia of the germinal epithelium. The appearance of columnar cells in the epithelial parts of a Brenner tumour is also well known. Teoh (1953) has shown that the histo-

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genesis of this tumour is similar to that of the granulosa-theca-cell group and not, as previously held, from the Walthard nests. The view held by some workers that these tumours arise by proliferation and ingrowth of the germinal epithelium would largely explain the concomitant finding of a Brenner tumour in the wall of a pseudomucinous cystadenoma. Teoh's work, however, supports the view that both theca and granulosa cells develop from the ovarian "stroma" which he regards as the parenchyma of the ovary, and this would seem to reduce the previously-mentioned finding to a coincidence. In addition, this case provides definite evidence against the widely-held view of a teratomatous origin for this tumour, as no teratomatous elements whatsoever were seen in serial sections, and surely they would be seen at this stage, were they present. The appearances seen in Figs. 5 and 6 also raise the possibility that some of the loculi in a multiloculated cystadenoma arise by multiple downgrowths from the surface rather than by budding, although it is likely that both processes take place.

Summary

A case of a very early pseudomucinous cystadenoma of the ovary is recorded, in which there is evidence that the tumour originates in the germinal epithelium.

How this dovetails with other aspects of ovarian oncology is briefly discussed.

My thanks are due to Dr. B. E. Tomlinson for permission to publish and for his criticism, to Mr. E. Manns for histological preparations and to Professor John McGrath and Mr. P. Fletcher for photographs.

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FIG. 1
A view of one side of the localized area of origin showing a rather papillary transitional zone between frank "germinal" and frank "pseudomucinous" epithelium. Haematoxylin and eosin. ×55.

FIG. 2
A view of the other side of the site of origin showing an abrupt change from "germinal" to "pseudomucinous" epithelium. Haematoxylin and eosin. ×55.

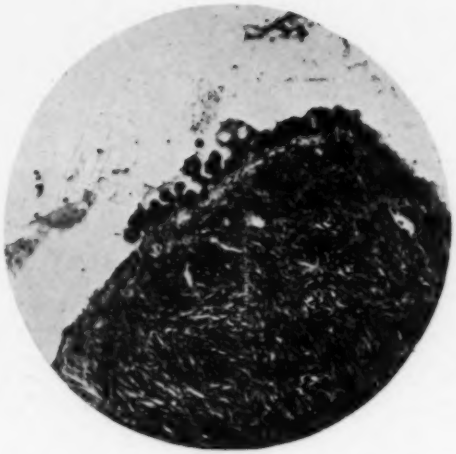

FIG. 3
A more highly magnified view of the area seen in Fig. 1. Haematoxylin and eosin. ×85.

FIG. 4
A high-power view of the abrupt change from one type of epithelium to the other, as seen in Fig. 2. Haematoxylin and eosin. ×320.

FIG. 5
Part of the surface of the ovary intermediate between Figs. 1 and 2 showing numerous clefts lined by "pseudo-mucinous" epithelium. Haematoxylin and eosin. ×85.

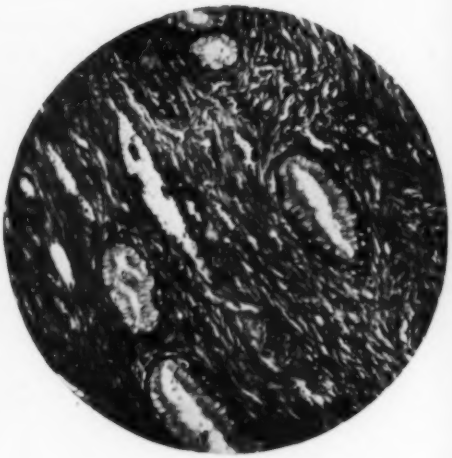

FIG. 6
Portion of the cortex one field below Fig. 5 showing clefts which have been cut off from the surface forming very small loculi. Haematoxylin and eosin. ×85.

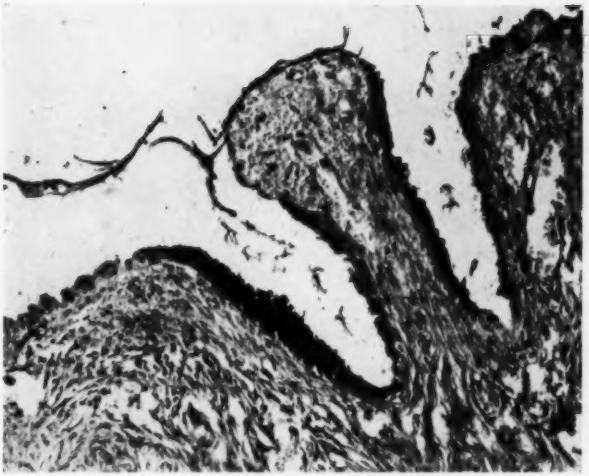

FIG. 7
Portion of the area seen in Fig. 1 stained to show the appearance of polysaccharide material in the cells. Periodic acid–Schiff. ×85.

THE PHENOTHIAZINE DERIVATIVES IN THE TREATMENT OF ECLAMPSIA

A Preliminary Report

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THERE is considerable divergence of opinion regarding the treatment of eclampsia. Since the disease is always associated with pregnancy one would imagine that rapid evacuation of the uterus, for example by Caesarean section, would be the best line of treatment, and indeed this was widely practised in the early part of the century. The results were most discouraging. Surgical trauma in an extremely ill patient led to severe shock and a high maternal mortality rate and because of this the surgical method of treatment fell into disfavour.

Eastman (1950) states "the immediate treatment of eclampsia today then is not concerned with the question of obstetric interference but is simply a matter of determining the particular form of conservative therapy which is to be employed".

However, delay in evacuating the uterus has its disadvantages. Peckham (1929) found that chronic hypertensive vascular disease was more likely to follow eclampsia when a prolonged period intervened between the first convulsion and delivery.

In recent years, with advances in methods of controlling the convulsions and improvements in anaesthetic techniques, some obstetricians will resort to Caesarean section if the patient's condition is satisfactory and she has had no fits for 24 hours.

Dewar and Morris (1947), having controlled the convulsions with bromethol, punctured the membranes in those cases in which the condition of the cervix seemed to predict a prompt uterine response. In severe cases, if such a response seemed unlikely, Caesarean section was performed.

The method of treatment of eclampsia is influenced to a certain extent by the existing facilities, particularly in regard to the amount of trained medical and nursing staff available. The Kandang Kerbau Hospital, where this investigation was carried out, serves a population of over a million people, and last year 20,000 women were delivered there. This number is greater than in any other hospital in the world, yet only a very limited number of doctors and nurses are available.

Since the majority of women will not attend antenatal clinics, the incidence of untreated pregnancy toxaemias is high, eclampsia is relatively common (88 cases were treated last year) and is frequently of a severe type. Furthermore the general health of many of the patients is poor due to malnutrition, worm infestation, and chronic anaemia.

The object of this investigation was to find a method of treatment which was safe, effective, and easy to carry out with the limited trained staff at our disposal. It was our belief that

evacuation of the uterus as soon as possible after the fits were controlled, offered the best chance of survival for both mother and child, provided the mother could be protected from the traumatic shock associated with operative delivery.

For some time we have been using a mixture of chlorpromazine hydrochloride and promethazine hydrochloride together with pethidine before major surgery (Smith and Fairer, 1953). From our observations we believed that these drugs would be useful in the treatment of eclampsia for the following reasons: (1) they produce prolonged and profound sedation (Cathala and Pocidalo, 1952; Courvoisier *et al.*, 1953); (2) they usually produce some fall in blood pressure (Laborit, Huguenard and Alluaume, 1952; Couthier, 1953; Dobkin, Gilbert and Lamoureux, 1954; Kent *et al.*, 1954); (3) the anti-adrenaline action of chlorpromazine and possibly the antihistamine action of promethazine appears to afford some considerable protection against the onset of traumatic shock (Fournel, 1952; Courvoisier *et al.*, 1953); (4) the work of Moyer *et al.* (1954) indicated that there were no deleterious effects of any kind on renal function following chlorpromazine.

Type of cases treated. Thirty consecutive unselected cases of eclampsia were treated by the method to be described. Of these, 16 were ante-partum, 5 were intra-partum and 9 were post-partum.

Method of Treatment

As a result of our experiences in the earlier cases in this series, we formulated this standard treatment. As soon as a case of eclampsia was seen, the following solution was prepared (solution No. 1); chlorpromazine 50 mg., promethazine 50 mg. and pethidine 50 mg. in 250 ml. of 5 per cent dextrose. This solution was given rapidly intravenously through an ordinary intravenous set with a wide bore transfusion needle. The first half of this solution (i.e., approximately 125 ml.) was poured into the vein with the drip screw control wide open and the second half was given at about 200 drops per minute, so that the whole amount was given within 10 minutes. This was followed immediately by solution No. 2 consisting of chlorpromazine 100 mg. with pethidine 50 mg. in 250 ml. of 5 per cent dextrose. The speed of the drip was set at 40 drops per minute and 10 minutes later the patient was catheterized, a Foley's catheter being left in the bladder. A vaginal examination was then performed and, if the patient was not in labour, an intravenous injection of atropine gr. 1/100th was given and she was prepared for Caesarean section. Very little anaesthetic was required during the operation and in most cases nitrous oxide and oxygen with gallamine triethiodide proved very satisfactory, but in a few cases, rather than risk any degree of hypoxia, minimal amounts of cyclopropane were added. The speed of the drip was adjusted so that by the time the operation was completed, solution No. 2 had all been given. From then on, the intramuscular route was used and chlorpromazine 100 mg. with pethidine 50 mg. was given by deep intramuscular injection every 6 hours for 3 or sometimes 4 injections. The first injection was usually given 2 hours after operation, but occasionally earlier if the patient showed any signs of restlessness.

If on examination the patient was definitely in labour, the membranes were stripped digitally from the lower uterine segment and then ruptured to hasten vaginal delivery.

On completion of solution No. 2, chlorpromazine 100 mg. with pethidine 50 mg. was given intramuscularly every 4 hours until delivery and then every 6 hours for 2 or 3 doses.

In cases of post-partum eclampsia solutions No. 1 and 2 were followed by chlorpromazine 100 mg. and pethidine 50 mg. intramuscularly every 6 hours for 4 doses.

Observations during Treatment

Within 5 minutes of the commencement of treatment, the patients presented the appearance of being in a deep sleep. This was quite dramatic in violently restless cases, which were rapidly brought under complete control. It was not necessary to precede solution No. 1 by any drug such as thiopentone to initiate control of the patient. The pallor characteristic of chlorpromazine administration replaced the plethoric appearance of those women who were not anaemic.

The initial drop in systolic blood pressure varied, the maximum being 126 mm. of mercury and the average 45 mm. of mercury. Even when the fall in blood pressure was considerable, it gave no cause for alarm, since it rose again within 3 hours. The only precaution necessary, if the blood pressure fell below the level of 100 mm. of mercury systolic, was to nurse the patient flat, instead of with the head of the bed raised, as is our usual practice in eclamptic cases.

The respiratory rate which on admission was frequently 40 to 50 per minute dropped to about 20 per minute and ventilation was adequate at all times. One patient reacted in a curious manner. When solution No. 1 was begun her respiratory rate was 55 per minute and after 5 minutes it dropped to 5 per minute for a period of less than 3 minutes, followed by normal respiration at 20 per minute. The patient was well oxygenated all the time. This was almost certainly a compensatory reduction in pulmonary ventilation following hyperpnoea and was not directly related to the drugs used.

An apparatus for the administration of oxygen under positive pressure was always available but it was never required.

Chlorpromazine depresses salivary and bronchial secretion, and our patients, after preliminary pharyngeal toilet as soon as they were adequately sedated, remained quite dry. We use atropine pre-operatively but it is doubtful if this is really necessary.

Control of Fits

In 11 of our 30 cases fits recurred after treatment had been started. In the earlier cases in this series we gave solution No. 1 much too slowly and it was necessary, in the more severe cases, to give small intermittent doses of thiopentone into the rubber tubing of the drip set to control the fits. In the later cases we avoided the use of thiopentone, giving only the standard treatment already described. In these later cases the fits if they recurred were quite different from those before treatment. Mainly, they consisted of mild twitches of the face and limbs which rarely lasted more than a minute and appeared to have little adverse effect on the patient. Furthermore, they occurred in patients who were heavily sedated and whose blood pressure was considerably lower than the pre-treatment level. Oedema was a very marked feature of most of our cases due to the associated malnutrition and hypoproteinaemia, and it is possible that cerebral oedema was the main cause of these minor fits. The intravenous administration of 200 ml. of 50 per cent dextrose appeared to minimize the chances of further recurrence of the fits.

The ideal treatment for eclampsia demands that there should be no recurrence of convulsions, even minor ones, and eventually we hope to solve this problem. Nevertheless, the complete recovery of the patient is the final test of the efficiency of any treatment and, from this small series, it would appear that our method compares very favourably with any other.

Condition of the Patients During and After Caesarean section

The excellent condition of the patients during and after operation was most marked. The complete absence of post-operative shock makes this method of treatment of eclampsia superior to any other we have tried.

Other Drugs Used During Treatment

We gave 200 ml. of 50 per cent dextrose intravenously at 80 drops per minute to produce diuresis. It was given twice a day during the first 24 hours and repeated during the second day if the urinary secretion was still not satisfactory. The following is a typical case which shows the efficiency of 50 per cent dextrose. The patient on the second day of her treatment was found to have secreted only 114 ml. of urine during a 10-hour period between 12 midnight and 10 a.m., so she was given 200 ml. of 50 per cent dextrose. The amount of urine excreted through the Foley's catheter then was as follows:

10.30 a.m.	85 ml.	1.00 p.m.	28 ml.
11.00 a.m.	200 ml.	1.30 p.m.	28 ml.
11.30 a.m.	28 ml.	2.00 p.m.	14 ml.
12 midday	28 ml.		
12.30 p.m.	28 ml.	Total for 4 hours	439 ml.

Fifty per cent dextrose also helps to counter-

act the effects of starvation from which all eclamptics suffer to some degree.

None of our cases developed venous thrombosis from this strong hypertonic dextrose solution nor from the solution containing the phenothiazine drugs.

Strophanthin, gr. 1/100, was given routinely every 6 hours for 24 or 48 hours, and penicillin, one mega unit twice a day, for 5 days.

Obstetric Management

Ante-partum Eclampsia

With one exception, in all cases in which labour had not commenced, pregnancy was terminated by Caesarean section as soon as the patient was adequately sedated. The exception was a young primigravida aged 17 years, 26 weeks pregnant only, with a "ripe" cervix. In her case, after stripping the membranes from the lower uterine segment and rupturing them, a pitocin drip was started. Good contractions began almost immediately and a non-viable foetus was delivered 6 hours later. If good contractions had not begun within 2 hours, we would have evacuated the uterus abdominally.

Intra-partum Eclampsia

All the intra-partum cases in this series were delivered vaginally, forceps being used if there was any delay in the second stage. We do feel however, that if there is any degree of inertia during the first stage, Caesarean section would be justified.

Results

Maternal Mortality

There was 1 maternal death, which occurred on the sixth day after admission and was not related to our standard eclampsia treatment. As will be seen from the following description, it could best be described as death from misadventure. The patient, a 29-year-old woman was not one of our booked cases. She had had 4 fits prior to admission, and on examination she was very oedematous and anaemic, her blood pressure was 140/108 and the urine was solid with albumen. The duration of pregnancy was estimated as 36 weeks, the cervix was not "ripe", and the presenting vertex was high and floating. Two hours after the commencement of the standard treatment, a lower segment Caesarean section was performed and a live 5-pound infant was delivered. Her post-operative course was completely uneventful. Urinary excretion was good, and albumen was absent as from the third post-operative day. Blood examination showed her haemoglobin to be only 38 per cent (Haldane), and on the fifth post-operative day a very slow blood transfusion was begun. Unknown to the nursing staff the drip suddenly increased in speed and the transfusion was given much too rapidly. The patient was found to be in great distress, dyspnoeic and cyanosed and with all the signs of congestive heart failure. Her blood pressure, which was 124/98 before the commencement of the transfusion, had risen to 200/140. Despite resuscitative measures she died 7 hours later, the cause of death undoubtedly being acute congestive heart failure precipitated by too rapid blood transfusion.

This was the only death in our series of 30 cases, giving a maternal mortality rate of 3·3 per cent.

Maternal Morbidity

In 2 cases complications occurred. One patient became mentally deranged and was transferred to a mental hospital but, after treatment for one month, she recovered and was discharged.

In the other case, the abdominal wound following a classical Caesarean section broke down, and had to be resutured.

The average length of stay in hospital for all our cases was 12 days.

Foetal Mortality

Thirteen infants did not survive, of which 3 were stillborn (one a case of hydrops foetalis), and the remainder were neonatal deaths. This gives the high foetal mortality rate of 43·3 per cent. However, in only 3 cases was the birth weight over 5½ pounds, and the average birth weight of the infants who failed to survive was only 4 pounds 2 ounces. Undoubtedly, prematurity was one reason for the high foetal mortality rate.

Summary

(1) A method of treating eclampsia with Phenothiazine derivatives is described.

(2) The series consisted of 30 unselected cases. There was one maternal death (maternal mortality, 3·3 per cent) and there were 13 foetal deaths (foetal mortality, 43·3 per cent). Prematurity was a major cause of the high foetal mortality rate.

(3) The method gave to the patients considerable protection against operative shock, and this enabled early evacuation of the uterus to be performed with minimum risk.

Acknowledgments

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HYPEREXTENSION OF FOETUS IN CASE OF TRANSVERSE LIE

BY

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A CASE of transverse lie with hyperextension of the foetus in the first stage of labour seems to be sufficiently rare to merit recording.

A 19-year-old primigravida from Gibraltar, of average physique, was admitted to the Maternity Centre, Dorset County Hospital, in labour at 9 p.m. on 24th February, 1955. She had been seen at the antenatal clinic regularly and the pregnancy had been normal, the presentation having been assessed as a vertex and the position LOA at each visit after the 32nd week of pregnancy. Her estimated date of delivery was 13th February, 1955.

On admission she gave a history of backache since 3.30 p.m. and a "show" at 4 p.m. The position was assessed by the midwife as a vertex LOA with the head engaged. No contractions were present at this time. She was given the routine preparation and put to bed. At 10.15 p.m. she was given sodium amytal, gr. 3 by mouth.

At midnight contractions commenced and by 1 a.m. they were occurring every 3–5 minutes. At 2.25 a.m. a vaginal examination was made—the cervix was 2–3 fingers dilated, the membranes intact and the presenting part high. At 3.15 a.m. the membranes ruptured and the profuse liquor showed some meconium-staining. The foetal heart-rate had dropped from 140 to 90 per minute, but increased to 140 again by 3.30 a.m. A further vaginal examination at 3.45 a.m. revealed the cervix 3–4 fingers dilated, the presenting part still high but no prolapse of the cord. The midwife was unable to identify the presenting part. Neither the house-surgeon nor the consultant obstetrician was able to identify the presentation by abdominal or vaginal examination. An X-ray was therefore taken and a reproduction of this is shown (Figs. 1 and 2). The position is seen to be a "chest" presentation with the spine hyperextended, and the head in the left upper quadrant of the abdomen with the occiput directed backwards.

Spontaneous delivery obviously could not occur and it was considered impossible to perform version. Contractions were still strong and there was no further evidence of foetal distress. At 7 a.m. 25th February, 1955, a lower segment Caesarean section was carried out under general anaesthesia. It was found impossible to deliver either the head or the breech through the transverse uterine incision. A fresh incision was made vertically upwards from the centre of it, converting it into an inverted T-shape and the infant was delivered breech first. The placenta, situated posteriorly, was delivered and the uterus and abdomen closed.

The female infant weighed approximately 7½ pounds and there were no anatomical abnormalities. She had a weak high-pitched cry for the first 2 weeks of life but otherwise behaved normally.

The puerperium was uneventful apart from some difficulty in establishing breast-feeding and on postnatal examination after 6 weeks the uterus was normal in size and position. There was no pelvic abnormality discovered to account for the unusual presentation, the cause of which therefore remains a mystery.

I should like to express my gratitude to Mr. D. Beaton for permission to publish this case and to Dr. J. G. F. Rose for permission to reproduce the radiographs.

FIG. 2

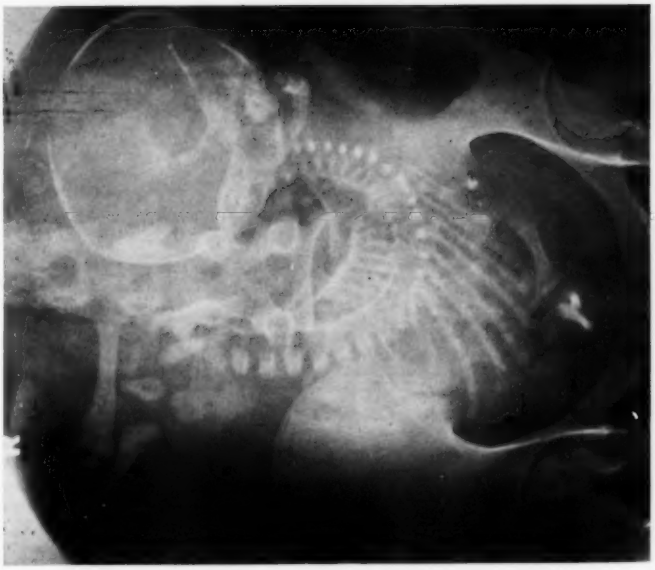

FIG. 1

LOUISE DE LA VALLIÈRE AND THE BIRTH OF THE MAN-MIDWIFE

BY

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Now, I'm sorry to say, At that time of day,
The Court of Versailles was a little too gay;
The Courtiers were all much addicted to Play,
To Bourdeaux, Chambertin, Frontignac, St. Peray,
Lafitte, Château Margaux, And Sillery (a cargo
On which John Bull sensibly (?) lays an embargo),
While Louis Quatorze Kept about him, in scores,
What the Noblesse, in courtesy, term'd his 'Jane Shores,'
—They were called by a much coarser name out of doors.—
This, we all must admit, in A King's not befitting!
For such courses, when followed by persons of quality,
Are apt to detract on the score of morality.
Ingoldsby Legends: "The Black Mousquetaire"

INTRODUCTION

THE art of midwifery is as old as woman herself, but until at least the sixteenth century it was practised almost exclusively by women. Scattered references to midwives occur in the Old Testament and the first one mentioned assisted at the second labour of Rachel, the wife of Jacob, who unfortunately died in labour (Genesis xxxv, verse 18). Another midwife delivered Tamar of twins (Genesis xxxviii, verse 27). Not all biblical references, however, are to reputable actions by midwives. In the first chapter of Exodus it is related that Pharaoh commanded two midwives to destroy all male children of Hebrew women. Fortunately for history, the midwives possessed sufficient conscience and independence to disobey this order.

In more recent times, at the fall of the Roman Empire, Eusebia, wife of the Emperor Constantius, was jealous of the fruitfulness of Helen, her husband's sister, the wife of Julian the Apostate, and she prevailed upon the midwife to murder Helen's child by cutting the umbilical cord too short. Further isolated accounts of the doings of midwives, both good and bad, occur throughout the Middle Ages, but certainly until the beginning of the seventeenth century midwives were little better than handy women.

Amongst the earliest of the celebrated and more knowledgeable midwives was Louise Bourgeois, who practised her art in France at the beginning of the seventeenth century. She was trained by the great Ambroise Paré himself, and in 1601 was responsible for the delivery of Marie de Medici, wife of Henry IV, the infant becoming the future Louis XIII. Two books would have been available to Louise Bourgeois upon which to base her practice. The *Rosegarten*, first published in 1513 and very soon afterwards translated into almost every European language (Figure 1), and secondly *La Comare* published in 1596 (Figures 2 and 3). Louise Bourgeois was, however, of an original turn of mind, and in 1609 she published her own book entitled *Observations on barrenness, abortion, fruitfulness, labour and disorders of women and newborn children*. Her practice became very large and fashionable, but came to an unfortunate end in the year 1627, when she delivered Madame de Montpensier, Duchess of Orleans, who died of peritonitis very shortly after the delivery. Following this disaster Louise Bourgeois fell into disgrace and died in poverty. In spite of this, her other book, entitled *Complete Midwives Practice enlarged*, appeared in an English edition dated 1659.

THE PROBLEM

The story of the rise of the art of midwifery from the time of Ambroise Paré and Louise Bourgeois onwards has been told often and well, and I do not intend to recount it again now. I wish to tell you of the entrance of men upon the obstetric stage. There are many who believe that this occurred gradually, and in fact occupied

about three centuries, the sixteenth, seventeenth and eighteenth. Others, however, believe that it was a sudden entrance precipitated by a single incident, alleged to have occurred in the middle of the seventeenth century. The incident concerns Louise de la Vallière, the first more or less permanent mistress of Louis XIV, and the delivery of one of their infants, probably the first. Before telling you of this, however, I think I should introduce Louise herself and some of her friends and contemporaries.

Louise de la Vallière (Figure 4) or, to give her her full name, Louise Françoise la Beaume la Vallière, was born in Touraine in August, 1644. Her father was Laurent de la Beaume la Blanc, Lord of la Vallière, and she lived during one of the most glorious epochs of French history. She was contemporary with the administrators Colbert and Louvois, the military architect Vauban and the soldiers Touraine and the Condés. She enjoyed the eloquence and literary glory of such men as Bossuet, Bourdaloue, Corneille, Molière, Racine and La Fontaine and she may have tried to understand the writings of the century's great moralists and thinkers, such as Pascal, Descartes and Rochefoucauld. Her father, however, died when she was 10 years old and her mother married for the second time the Marquis de Saint Rémy, who was first maitre d'hôtel to Gaston, Duke of Orleans. Louise's adolescence, therefore, was spent in luxurious surroundings.

The Duke of Orleans died in 1660 and the Dowager Duchess removed to the Luxembourg palace taking both Louise and her mother with her as maids of honour. In the following year Louis XIV's brother Philip became Duke of Orleans, and married Henrietta of England, the daughter of Charles I. Louise thereupon became attached to the household of Henrietta and was used by her as decoy to cover her illicit relationship with Louis which had just started. It was, however, about this time that Louise herself attracted the amorous attentions of Louis. Her contemporaries tell us that she had a good appearance (Figure 5), but her nose and neck were too long, her teeth were defective, her arms were perhaps a little too heavy but she looked well on horseback! Paul Heuzé put it: "Elle boite un peu, mais elle danse bien" (She limps a little, but she dances well). Louis himself (Figure 6) was no beauty, but had sufficient charm and personal magnetism to sweep half the court off its feet and into his bed. Louise de la Vallière undoubtedly fell sincerely and wholeheartedly in love with him, and it is with the obstetric results of her infatuation that I wish to deal.

There seems to be some doubt about the exact number of children which she bore to Louis XIV, the order in which they were born, and who delivered them. The originator of most of this confusion appears to be the French obstetrician Jean Astruc (Figure 7), who was not born until 1684. He first saw the light of day in a Huguenot manse, was baptized in a Protestant church, was brought up a Roman Catholic and continued to practise that religion until his death. He took his M.D. in Paris in 1703 and was appointed to the Chair of Anatomy at Montpelier in 1717. In 1731 he removed to the Chair of Medicine in the Royal College of Paris, and in 1745 he took over the task of lecturing to the midwives of Paris on Medicine. His book on midwifery was first published in England in 1766, which was the year of his death (Figure 8). In the introduction to this book he states that Louise de la Vallière's first infant was born on 27th December, 1663, was christened Louis, and survived less than 5 years. As to the details of the delivery, Astruc tells us that it was conducted by a certain Jules Clément who was smuggled into Louise's house at dead of night, and was never allowed to know the identity of his patient. He tells us further that Clément was also summoned to all Louise's subsequent confinements which numbered at least a further three, and he claims that it was this first successful delivery of Louise de la Vallière that influenced members of the French Court to employ men as midwives when they wished to keep their illicit deliveries secret. In other words, this particular delivery set the fashion for the employment of man-midwives. We are also told that in recognition of the successful outcome of this delivery Louis XIV conferred the title of "Accoucheur" upon Clément. This story, without verification, has been copied by several authors since that date; in the early part of the present century Sir Alexander Simpson repeated

it, and it subsequently found its way into the *Encyclopaedia Britannica*.

I would like now to examine the truth of the story of Louise's first delivery from several points of view. Firstly, was a male child called Louis born to la Vallière on the 27th December, 1663? Secondly, was this child delivered by Jules Clément? Thirdly, if Clément did in fact conduct the delivery, was it in recognition of this that Louis conferred the title of "Accoucheur" upon him, and was this delivery the starting point of the popularity of the man-midwife? There seems to be very considerable doubt about the date of the child's delivery and also its name. We are told by Colbert, one of Louis' closest confidants and organizer of many of his private doings, that Louise was delivered of a boy on 19th December, 1663. The child almost immediately passed into the care of foster parents and died within a year. Colbert also informs us that the infant was delivered by a man, Monsieur Boucher, and christened Charles. This confusion in the name is perhaps a minor complication with which we need not concern ourselves, but Colbert also fails to mention any undue secrecy. The oft repeated statement that the infant was delivered by Jules Clément rests almost entirely upon the evidence of Astruc. His account of the incident was written at least 80 years after it occurred.

Jules Clément

Jules or Julian Clément was born in Provence in either 1648 or 1650. He went to Paris and studied under Jacques le Faure and subsequently married le Faure's daughter. Clément became a well-known midwife and was recommended by Fagon, physician to Louis XIV (Figure 9), to deliver the Dauphiness which he did in 1686, and perhaps also in 1682. He was so successful in practice that Louis XIV raised him to the peerage in 1711 on condition that he would continue to give his services free to the poor. He journeyed to Madrid in 1713, 1716 and again in 1720 to deliver the Queen of Spain. He died in 1728 or 1729, and a quick glance at these dates shows that he was only 13 or 14 years old at the time of Louise de la Vallière's first confinement. Even allowing for precocious development and early medical qualification it would obviously have been quite impossible for him to have been present at this delivery. In his recent book *Eternal Eve* Harvey Graham also points out the impossibility of Clément being present at the delivery owing to his extreme youth.

If, therefore, Clément did not conduct this delivery, who in fact did? The famous Colbert, who was contemporary with all these happenings and has left very full writings behind him, states categorically that the delivery was conducted by "l'homme Boucher", and I cannot see any reason for doubting the truth of this story, but Boucher remains a man of mystery and it has been impossible for me to find out anything about him. In view, however, of Colbert's clear description of the event, there does not appear to be any real reason for doubting his existence. Garrison, in his *Introduction to the History of Medicine*, manages to confuse the issue further by mentioning the first delivery of Louise de la Vallière in two different parts of his book. In the first instance he states that Clément was responsible, in the second Boucher. Harvey Graham, having admitted that Clément could not have been responsible for the delivery because of his age, states that it was carried out by a midwife called Marguerite Boucher. What evidence he has for this statement, however, is very difficult to find out and, when he tells us that the Queen, Marie Thérèse, was delivered in 1667 by a man-midwife called Bouchet, it is easy to see the importance of going back to the original descriptions. There is good evidence that all Marie Thérèse's deliveries were conducted by women and the senior female midwife of that day does appear to have been called Boucher. It may be that the name Boucher was given to the *man* who delivered Louise de la Vallière to cover up his real identity. There is no mention of anyone called Boucher amongst Louis' medical advisers. It is interesting here, however, to note the composition of his staff. It consisted of a senior physician and twelve junior men with diminishing degrees of responsibility. The senior physician for a large part of the reign was Fagon (Figure 10). There was also a senior surgeon and 8 other surgeons on the staff, 4 apothecaries and 4 assistant apothecaries and 17 other appointments including 2

"cutters for stone", 2 barbers, and a dentist. It seems hard to understand why, with such a large medical staff, and all the obstetric happenings in Louis' court, there was not the appointment of at least one regular midwife. The names of the holders of most of these offices have been lost to posterity, but we do know that the Royal Physicians were named Vallot, d'Aquin and Fagon.

The Solution

I should like to say in summary that Louise de la Vallière's first delivery almost certainly took place on the 19th December, 1663; a baby boy was delivered by a man-midwife called Boucher who had been employed by Colbert. This infant probably survived less than one year. Colbert's motive in calling in Boucher was very likely in order to preserve secrecy, as the intrigue between la Vallière and Louis had probably not yet reached the Queen's ears. The further obstetric history of la Vallière, however, may be of some importance to this story. Another boy was born in 1665 which once again survived less than a year, a girl in 1666, and another boy in 1667. It is Astruc who again recounts that Clément was called in for all these deliveries, but in Colbert's memoirs it is made quite clear that Boucher delivered at least two out of the three infants. I would like to tell you something about the baby girl born in 1666, as she may provide an explanation for some of the confusion. The infant was christened Marie-Anne de Bourbon, was known afterwards as Mademoiselle de Blois, and was one of the few of Louis' children to survive into adult life. She married when quite young and became Princess de Conti. Bear in mind the name Mademoiselle de Blois for a few moments if you will.

In the year 1675, after at least two unsuccessful attempts, Louise de la Vallière finally managed to quit the court and became a Carmelite nun. Since about 1668 her place in the king's affections had been usurped by Madame de Montespan, who was born in 1640 to one of the oldest families in France, and was christened Françoise-Athenais (Figures 11 and 11a). She came to court in 1661 about the same time as la Vallière, and in the following year married Monsieur de Montespan. In her unscrupulous efforts to win the king's affection, she quickly became a devotee of Black Magic, a worshipper at the Black Mass and one of the most celebrated customers of La Voisin, the infamous French witch. La Voisin's magic apparently worked, because by 1668, as I have already said, Madame de Montespan was firmly entrenched in Louis' affections. Her obstetric history is better authenticated than la Vallière's and she bore nine children in all, two to her husband and seven to the king. Her husband's children were born in 1663 and 1664. She bore the king's first child in 1669, a girl who survived for three years. She bore a son in 1670 and we are told by Garrison and Harvey Graham that this delivery was conducted by Clément. This is not difficult to believe, as, apart from Mauriceau, Clément was the most distinguished male exponent of the art of obstetrics in France at this time. Montespan had another son in 1672, a girl in 1673, and another girl in the following year 1674. I want, however, specifically to direct attention to the next child she bore the king, a girl born in 1677, who also became known as Mademoiselle de Blois. There is evidence for believing that all these deliveries were conducted by Clément, including Montespan's last in 1678. It seems quite possible that confusion has arisen between the two infants known as Mademoiselle de Blois, one born to la Vallière in 1667, and the other one to Montespan, ten years later. Clément almost certainly delivered the one born to Montespan, and the tacit assumption has been made that he also delivered the Mademoiselle de Blois born to la Vallière in 1667. Montespan's Mademoiselle de Blois was obviously an engaging child (Figure 12), so much so that she subsequently married the Duke of Orleans, who became Regent of France in the following reign. Before I attempt to resolve these difficulties please allow me one further digression.

We know that Clément was a distinguished man-midwife but throughout his life he contributed nothing to the obstetric literature of his day. When, however, he was at the height of his powers in 1670, and responsible for the obstetric care of the reigning favourite, Madame

FIG. 2
A patient about to undergo Caesarean Section.
From the first edition of *La Comare*, 1596.

FIG. 1
Midwife examining patient seated on a birth chair.
From a copy of the first edition of the *Rosegarten*,
1513.

G.-P.-L.

FIG. 3
The "hanging legs" position for delivery in cases of contracted pelvis. From first edition of *La Comare*, 1596. (Compare with position described by Walcher in 1887.)

FIG. 4
Louise-Françoise, Duchess de la Vallière.

G.B-L.

FIG. 5
Duchess de la Vallière.

FIG. 6
Louis XIV as a young man.

G.B-L.

FIG. 7
Jean Astruc, 1684–1766.

ELEMENTS
OF
MIDWIFRY.

Containing the moſt Modern and Succeſsful
METHOD OF PRACTICE
IN
Every different KIND of LABOUR.

WITH
A ſhort HISTORY of the ART of MIDWIFRY,
AND
An Anſwer to a CASUISTICAL LETTER, on the Conduct of ADAM and EVE, at the Birth of their firſt CHILD.

By J. ASTRUC,
Profeſſor Royal of PHYSIC, in the Univerſity of PARIS, and Phyſician to the King of FRANCE.

Tranſlated, with ADDITIONS and explanatory NOTES,
By S. RYLEY,
Member of the Corporation of SURGEONS in LONDON.

LONDON:
Printed for S. CROWDER, at the Looking-glaſs; and J. COOTE, at the King's-Arms, in Pater-noſter-Row.
MDCCLXVI.

FIG. 8
Title-page from first English edition of Jean Astruc's *Elements of Midwifery*, 1766.

FIG. 9
Guy Fagon, for many years senior physician to Louis XIV.

FIG. 10
Statuette of Fagon as an old man.

G.P.L.

FIG. 11
Françoise-Athenais de Rocheouart, Marchioness de Montespan.

FIG. 11a
Françoise-Athenais, Marquise de Montespan.

G.B-L.

FIG. 12
Mlle de Blois, daughter of Mme de Montespan. Born 1677. Became Duchess of Orleans by marriage.

ANATOMICAL EXERCITATIONS,

Concerning the

GENERATION

Of Living Creatures:

To which are added Particular Diſcourſes, of *Births*, and of *Conceptions*, &c.

By *WILLIAM HARVEY*, Doctor of *Phyſick*, and Profeſſor of *Anatomy*, and *Chirurgery*, in the COLLEDGE of Phyſitians of *LONDON*.

LONDON,

Printed by *James Young*, for *Octavian Pulleyn*, and are to be ſold at his Shop at the Sign of the Roſe in St. *Pauls* Church-yard. 1653.

FIG. 13
Title-page from William Harvey's famous book on Generation, published in 1653.

G.B-L.

FIG. 14
Frontispiece from the third edition of Mauriceau's book entitled *Traité des malades des femmes grosses*, 1681.

FIG. 15
The Nativity, showing an obstetric stool standing in the corner of the delivery room. (Paris, 15th century.)

de Montespan, Hugh Chamberlain was in Paris visiting François Mauriceau. Chamberlain had crossed from London where Harvey's book *de Generatione* had been published not twenty years before, and was at the time the most modern obstetric textbook in English (Figure 13). It did not perhaps provide quite as much basic information as Chamberlain thought necessary for the practising midwife. Chamberlain was undoubtedly one of the foremost man-midwives of his day, quite apart from the fact that he was a member of the family that kept the secret of the obstetric forceps. His object in visiting Paris was to meet François Mauriceau, demonstrate his forceps, and perhaps even succeed in selling them to Mauriceau. He hoped also to persuade him to allow publication of his book in English.

The story of the highlight of this visit is well known. Chamberlain attempted to deliver with forceps, a rickety dwarf, a patient of Mauriceau's in the Hôtel Dieu. Notwithstanding his best efforts he failed and the patient died undelivered forty-eight hours later. In spite of this disaster, Mauriceau was apparently favourably impressed by Chamberlain because he allowed him to arrange for the publication of his book. The first English edition appeared in 1676 (Figure 14). Mauriceau had been born in 1637 and had learnt his midwifery in Paris at the Hôtel Dieu. He was responsible for many innovations, including the one of delivering his patients in bed rather than on an obstetric stool, which was in common use up to his day (Figure 15). He was a brilliant teacher, wrote extensively, and was the first person to correct the erroneous view that the pelvic bones separated in labour. His was also one of the earliest references to tubal pregnancy and also to difficult labour due to involvement of the umbilical cord. According to Eastman, however, Mauriceau was responsible for the teaching that posterior positions of the occiput always caused difficulty and often danger, a view which was reinforced by Smellie in the subsequent century, and believed implicitly for over one hundred years until Naegele pointed out the error. Mauriceau was the foremost French academic obstetrician of his day, was one year older than Louis XIV himself, and, in view of his age and eminent position in the obstetric world, it is extremely difficult to believe that he was not at least consulted over some of the court obstetric cases. I must frankly admit, however, that this is pure conjecture; there is no existing evidence linking Mauriceau with any of the doings of the French court. Could he perhaps be the mysterious "l'homme Boucher" to whom Colbert refers?

Envoi

I think I should now tell you what finally happened to the principal characters involved in this story. La Vallière had retired to her Carmelite convent in 1675. There she lived an exemplary life in spite of the fact that she was visited on several occasions by Madame de Montespan and Montespan's successor, Madame de Maintenon. She underwent great penances and died full of holiness in 1710. The Queen, Marie Thérèse, died in 1683 and almost immediately Louis married Françoise d'Aubigné, widow of the poet Scarron, who was subsequently known as Madame de Maintenon. In spite of this personal reverse, Madame de Montespan continued to live at court until 1691 when she retired to a cloister and died in 1707.

From the time of the death of his Queen onwards, Louis was involved in almost continuous warfare. He revoked the edict of Nantes in 1685, and instituted many punitive measures against the Huguenots. In these he was aided and abetted both by Madame de Maintenon and the Jesuits, but curiously enough the Pope of the day, Innocent XI, was against Louis and gave his wholehearted backing to William of Orange, the acknowledged leader of the anti-Louis opposition. This was almost certainly the only time that William and the Pope were on intimate terms and on the same side of the fence! In 1690 Louis went to war against the League of Augsburg, which was headed by William of Orange. This war lasted until 1697 when Louis was forced to recognize William as the legal King of England. Three years of peace followed but in 1700 Louis was again at war over the question of a successor to Charles II of Spain who had just died. This war dragged on and on and the last few years of Louis' life were plagued by a series of battles fought unsuccessfully against the Duke of Marlborough. Louis died

in 1715 at the age of 77, having ruled as King of France for 72 years.

So with the death of the last of the principal characters involved we are free to take stock of the position. We know that at least until the middle of the sixteenth century the art of midwifery had been practised almost exclusively by women. There are medical historians, however, who believe that the entrance of man into this almost exclusively female province was due entirely to the successful delivery of the first child of Louise de la Vallière by Clément in 1663. Astruc was almost certainly responsible for the popularity of this story, but he wrote his account at least 80 years after the event, and Jules Clément was at the most 14 years old when la Vallière's first child was born. All of Louise's deliveries were almost certainly conducted by a man named "Boucher". Clément was however almost certainly responsible for most, if not all, of Madame de Montespan's deliveries, and it may well be that his delivery of the child that subsequently became known as Mademoiselle de Blois has given rise to such confusion, when we remember that la Vallière had a daughter ten years earlier, also known as Mademoiselle de Blois. The title of "Accoucheur" almost certainly was conferred upon Clément, but it is difficult to be certain whether it was in recognition of the first delivery of Madame de Montespan in 1670, or the delivery of the Dauphiness in 1682, as Garrison would have us believe. I am inclined to the view that man's rise to a position of obstetric superiority was a slow one. Ambroise Paré in the sixteenth century prepared the way for this by popularizing the operation of external version. Then the various obstetric comings and goings of the Court of France in the seventeenth century had to be conducted with a measure of secrecy. This also enabled men to get a firm handhold on obstetrics. This superiority became unshakable with the development and revelation of the obstetric forceps. Man's obstetric beginnings may perhaps be in doubt but his present and future seem assured.

The pleasure that I have derived from writing this short essay has been heightened by the interest and kindness of many friends who have both read and commented upon it. I owe a special debt of gratitude to Dr. G. R. C. Keep for introducing me to Thomas Ingoldsby and his *Legends*.

I should like to thank Dr. A. H. Curtis for permission to reproduce the portrait of Jean Astruc, and also the W. B. Saunders Company for permission to use Figures 7 and 14. Figure 10 appears by permission of Routledge & Kegan Paul, Ltd.; the original statue is in the Carnavalet Museum, Paris.

Most of my remaining illustrations are taken from the *Galerie des memoires du Duc de Saint Simon*.

Finally I should like to thank Professor J. J. Pritchard for allowing me to use the photographic facilities of the Department of Anatomy, Queen's University, and also Mr. S. McKearney, technician in the Department of Anatomy, for his excellent work on the illustrations.

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JOHN BRAXTON HICKS, BIPOLAR VERSION, AND THE CONTRACTIONS OF THE PREGNANT UTERUS

BY

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TURNING the foetus *in utero* remained for many years one of the principal methods of coping with a variety of major obstetrical complications. It was frequently resorted to in the management of cephalopelvic disproportion, malpresentation, placenta praevia, and even eclampsia; only in the present century has it been supplanted by improved methods of therapy for these conditions.

Until the second half of the last century only one method of version was used, the internal podalic, associated with its well-known limitations and risks. External version was then proposed as a method for changing the polarity of the foetus from head to breech, but its shortcomings proved too great for general acceptance. Hicks's (1860) method of combined internal and external, or bipolar, version was received as one of the major contributions to obstetric practice in his generation.* It has been known ever since as the Braxton Hicks version and is still resorted to occasionally by a few obstetricians. His original description, accompanied by illustrative diagrams (Fig. 2), compares his new method with external version:

"Before I had read of [external version] . . . I had already employed a method, combining the power possessed by external manipulation with the power and certainty derived from pressure and touch through the cervix, and which . . . appears to be more satisfactory, and more easily managed by those who have not given, nor are able to give, to the external diagnosis of foetal position such care and skill as Professor Carl Esterle; for even Martin, of Jena, insists that by his plan it is necessary—first, that immediate delivery be not called for; second, that there be a capacious pelvis; third, that there be active pains; fourth, that the child be living. From the following remarks and illustrative cases, I think I shall show sufficiently that the method I have employed does not require such conditions. Accepting, then, the valuable fact, that the foetus in utero can be turned without the necessity of the entry of the hand into the uterus, I shall now prove the extensive applicability of the plan I have adopted to labour in its various complications."

Proceeding with a comparison of his method with internal podalic version, Hicks wrote: "In considering, secondly, the general advantages of this operation over the ordinary method, I disclaim all intention of unnecessarily deprecating an exceedingly valuable and ancient operation—one which has saved numberless lives, and one with which, at present, we cannot dispense. Still, if it can be shown that in a considerable number of cases requiring version, the operation can be accomplished as quickly, or even more so, without the necessity of introducing the hand into the uterus, with the exception of one or two fingers passed a little way into the os, I am sure that such a modification of this more or less hazardous operation will recommend itself without any panegyric on my part. For in that case it will readily be perceived that we shall avoid:

"1. The addition of the hand, and perhaps arm, to the uterine contents; and the irritation, present and future, caused by it.

* A method for converting a shoulder to a cephalic presentation by combined intra-uterine and external abdominal manipulation was described in 1854 by M. D. Wright of Cincinnati, who credited the even earlier use of a similar method for correction of shoulder presentations to Professor Flamand of Strasbourg. (Wright, M.D. *Difficult Labors and Their Treatment*. Cincinnati. Jackson, White & Co.'s Mammoth Steam Printing, 1854.)

FIG. 1
John Braxton Hicks (1823–1897).

men downwards, the knees of the fœtus are opposite the os uteri; and if the os is large enough to introduce a finger, the knee can be hooked down and the presentation secured. Thus it is evident that it is merely necessary for the fœtus to assume the above position, where delivery by knee or foot is sought for, or where we wish that the delivery may be at our command. I shall defer alluding to version of cephalic into pure breech presentation till I speak of the method of operation.

The next fact to be borne in mind is that, should the fœtus, either naturally or by the method to be described, present by its back to the os uteri, the case would be very rare in which one side or the other was not the more dependent, and consequently one or the other knee be within finger-reach of the os.

The third fact needful to reflect upon in this, that the shape of the cavity of the fully-developed uterus being oval, with the long axis placed vertically, the tendency of the slight pains towards the end of pregnancy is to place the longer axis of the fœtus in a corresponding direction; or, in other terms, to cause it to present by the head or breech: so that if the fœtus be at any time situated transversely, a slight preponderance of force in either direction will be sufficient to determine the ultimate presentation. It will be thus perceived that, the head being heavier than the pelvic extremity, the natural tendency of a spontaneous rectification will be to head presentation; but at the same time it would have taken but little force to have caused it to rise to the fundus.

Having premised these considerations, we will discuss the other facts as they arise in the application of the above principles, taking for granted that it is admitted possible to turn the fœtus in utero from the outside. The method I have found successful, and very easy of application, is conducted thus:—We will suppose the simplest condition, a case where the uterus is passive, membranes unbroken, the liquor amnii plentiful, the os uteri expanded sufficiently to detect the presentation, which is cephalic, and in the first or fourth position (occiput to left side); the patient is in the ordinary position, the trunk curved forwards as much as possible, to relax the abdominal muscles. Introduce the left hand, with the usual precautions, into the vagina, so far as to fairly touch the fœtal head, even should it recede an inch. (This generally requires the whole hand.) Having passed one or two fingers (if only one, let it be the middle finger) within the cervix, and resting them on the head, place the *right* hand on the *left* side of the breech at

FIG. 1.

the fundus uteri, as shown at Fig. 1. Employ gentle pressure and slight impulsive movements on the fundus towards the right side, and simultaneously on the head towards the left iliac fossa. In a very short time it will be found that the head is rising and at the same time the breech is descending. The shoulder is now felt by the hand in place of the head, as in Fig. 2; it in like manner is pushed to the left, and at the same time the breech is depressed to the right iliac fossa. The

FIG. 2.

fœtus is now transverse; the knee will be opposite the os, and, the membranes being ruptured, it can be seized, as at Fig. 3, and brought into the vagina.

Having now the labour at command, the case must be treated according to the circumstances which called for turning. In

FIG. 3.

obedience to the law above stated, when the fœtus is placed transversely, a slight impulse will determine the final position of the head. When the leg is seized, therefore, it is advisable

FIG. 2
A page from Hicks's paper on bipolar version, with illustrative diagrams.

ON THE CONTRACTIONS OF THE UTERUS THROUGHOUT PREGNANCY: THEIR PHYSIOLOGICAL EFFECTS AND THEIR VALUE IN THE DIAGNOSIS OF PREGNANCY.

By J. Braxton Hicks, M.D. Lond., F.R.S.

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I am anxious to direct the attention of the profession to a point connected with the pregnant uterus, which has been almost entirely and surprisingly overlooked, as far as my researches into authors lead me to believe. Perhaps the following quotation from Dr. Tanner's work 'On the Signs and Diseases of Pregnancy,' p. 118, 1860, will best show the state of our knowledge and the authors who have alluded to the subject:

"More than twenty years since Mr. Ingleby observed that 'in advanced pregnancy the uterus, when moderately grasped and rubbed, slightly hardens and almost instantly regains its yielding condition.' Dr. Oldham has since pointed out that this power of contraction possessed by the uterus may be taken as a trustworthy characteristic of pregnancy; for he states that the large gravid uterus alters in a marked manner, under the influence of pressure, from a state of flaccidity to one of tension. Thus, if we expose a pregnant woman, the outline of the tumour is seen to be less defined before manual examination than it becomes afterwards; for on applying the hand, the tumour which at first is felt soft and ill-circumscribed, rapidly assumes a tense rounded form, becoming firm and resisting. According to Dr. Oldham no other tumour but the pregnant uterus possesses the power of altering its form when irritated by palpation; but I must here beg to differ in opinion from this gentleman. Only a short time since I was examining the abdomen of a poor woman suffer-

Fig. 3

Title page of Hicks's paper on the uterine contractions now associated with his name.

"2. Entry of air within the uterine cavity.

"3. Liability to rupture of the uterus.

"4. Much of the pain and distress felt in the ordinary plan.

"5. The removal of the coat, and baring the arm of the operator; and, as a minor consideration,—

"6. The fatigue and pain endured by the operator while the hand is in utero."

Hicks concluded his paper with mention of the conditions in which his method of combined version could be used to advantage, and appended reports of 5 cases in which it was employed in the treatment of placenta praevia:

"From the foregoing remarks, it will be readily seen that it can be applied at the earliest period a malpresentation is detectable. As soon as the finger can enter the cervix, so soon can version be performed, converting all forms into breech presentations. In malpositions of the head, perhaps it may be found capable of improving its position without having recourse to complete podalic version; in puerperal convulsions, diminishing the great risk in such cases from the addition of the hand to the contents of the uterus; in narrow brims when version is decided upon, it will save the pressure upon the os uteri against the projecting parts of the brim . . . I shall for the present confine myself to the advantages this method gives us in placenta praevia—at least, in every form of partial insertion."

It was this last condition for which the Braxton Hicks method of version proved most valuable, its wide adoption in the management of placenta praevia leading to a reduction in maternal mortality from 30 per cent to 5 per cent (Cullingworth, 1898). In a case of severe haemorrhage, with the cervix dilated only sufficiently to admit 1 or 2 fingers, "anything", he wrote, "which gave the practitioner some power of action was to be earnestly welcomed; anything better than to stand with folded arms, incapable of rendering assistance for hours and even days, every moment of which might be carrying the sinking and suffering patient nearer to the grave . . . Turn, and if you employ the child as a plug the danger is over. Then wait for the pains, rally the powers in the interval and let nature, gently assisted, complete the delivery."

Important as was Hicks's method of bipolar version to the obstetrics of his day, far more basic and enduring was his later description of the contractions of the uterus during pregnancy (Hicks, 1871), now universally known as Braxton Hicks contractions. This classical contribution to obstetrical literature is a masterpiece of clinical observation and inductive reasoning. The following paragraphs from it are sequential but not necessarily consecutive:

"It was a source of difficulty to the older obstetricians to explain how that, at a certain time, namely, at the full period of pregnancy, the uterus, passive up till then, began all at once to acquire a new power, that of contracting; forgetful that, long before the full period had arrived, the uterus has the power to expel the foetus, and under mental excitement or local stimulation, attempted to do so frequently.

"But after many years' constant observation, I have ascertained it to be a fact that the uterus possesses the power and habit of spontaneously contracting and relaxing from a very early period of pregnancy, as early, indeed, as it is possible to recognize the difference of consistence—that is, from about the third month."

". . . If, then, the uterus be examined without friction or any pressure beyond that necessary for full contact of the hand continuously over a period of from five to twenty minutes, it will be noticed to become firm if relaxed at first, and more or less flaccid if it be firm at first. It is seldom that so long an interval occurs as that of twenty minutes; most frequently it occurs every five or ten minutes, sometimes even twice in five minutes. However, in some cases I have found only one contraction in thirty minutes. The duration of each contraction is generally not long, ordinarily it lasts from two to five minutes. When the uterus is irritable or has been irritated it lasts longer than this; under particular circumstances . . . it may assume an almost continuous action analogous to that which is noticed after long obstructed labour."

". . . The consistency with which these contractions of the uterus have always occurred to me leaves no doubt on my mind but that it is a

natural condition of pregnancy, irrespective of external irritation.

"In a general way the pregnant woman is not conscious of these contractions of the uterus, but sometimes she will remark that she has a tumour in her lower abdomen, thinking it a constant thing; but another will observe that she has a swelling sometimes, but which vanishes at other times. But occasionally it happens that the uterus is more than usually sensitive, and that the contractions are accompanied by pain; and then on examination it is found that each pain she complains of is co-incident with a contraction."

". . . We need not, with the cognizance of this intermittent action, any longer wonder how it is that suddenly a new function is given to the uterus at the end of the ninth month; it is already in active exercise, not perceptible to the pregnant woman, though it is to the examining hand. We also find in this frequent contraction an explanation of the change of note in the uterine souffle. Every one conversant with the sounds of pregnancy has noticed that while listening to the sounds formerly called placental, but now acknowledged to be uterine, the loud sonorous sound has become gradually higher till it is almost a shrill piping musical one. It has puzzled many authors to explain this, but one sees no difficulty in it; the diameters of the uterine sinuses are slowly reduced by the contraction of the walls, the rapidity of the rush of the blood increased, and the pitch of the sound consequently heightened. It also explains the phenomenon of 'after pains', in which we see a continuation of the same intermittent movements after removal of the exciting cause . . ."

Hicks's views concerning the "effects or uses" of these contractions have not been improved upon to this day:

"In the first place, it will provide for the frequent movement of the blood in the uterine sinus and decidual processes, for as the sinuses of the uterus are so much larger than the supplying arteries, the current is more slow in them than in the ordinary systemic veins. The contraction of the walls through which the sinuses meander tends to send the current onward, and to act somewhat as a supplementary heart.

"Besides this, it facilitates the movement of the fluid in the intervillal space of the placenta, or in that which is called the placental sinuses . . ."

"In the second place, the uterine action adapts the position of the foetus to the form of the uterus . . ."

Hicks also called attention to the value of the contractions in establishing the diagnosis of pregnancy:

"For the last six years and upwards I have made use of the intermittent action of the uterus as the principal symptom upon which I have depended in the diagnosis of pregnancy. I am not aware that I have been less successful than others in determining the existence of pregnancy; on the contrary, I have felt myself at an advantage in the possession of an additional sign to make up the deficiency or temporary inapplicability of the others; as, for instance, when external noise prevents the heart sounds from being heard."

John Braxton Hicks, one of the most illustrious figures in British obstetrics, was born in Rye, Sussex, in 1823 (Cullingworth, 1898; Mundé, 1898). He studied medicine at Guy's Hospital, where he won many prizes and honours, receiving his M.D. degree in 1851. He then entered general practice in Tottenham in partnership with Mr. W. Moon. Later devoting himself to obstetrics, Hicks was appointed to progressively higher teaching posts at Guy's Hospital, and was finally made Obstetric Physician to St. Mary's Hospital as well. He held diplomas from the Royal College of Surgeons and the Apothecaries' Society, was a Fellow of the Royal Society and the Linnaean Society, a member of the Hunterian Society, of which he was President in 1879, and a founding member of the Obstetrical Society of London, which he served as President in 1871 and 1872. He retired from practice in 1894, and died at the Brackens, Lymington, 28th August, 1897, at age 74. His bibliography contains 133 medical titles and 23 other scientific papers on non-medical subjects, outstanding among the former being his studies on uterine inertia and the state of the uterus in obstructed labour. The name of Braxton Hicks is also associated with a modified cephalotribe, which became the standard instru-

ment of its type in England. The breadth of his interests, which encompassed botany and zoology, is shown by the titles of some of his publications, such as *Lichen Mosses and Unicellular Algae*, *On certain Sensory Organs in Insects Hitherto Undescribed*, and *On the Homologies of the Eye and Its Parts in Invertebrates*.

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ANHYDRAMNIOS*

Preliminary Report

BY

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THE average medical dictionary contains between forty and fifty thousand words. The student's task is the heavier in that many of these words are superfluous, and many are ambiguous. One would not, therefore, have the heart or the temerity to add to such a list, unless the grounds for doing so were unassailable. However, there is no word, as far as I know, to denote total lack of liquor amnii—a condition which does occur, be it rarely. The word anhydramnios describes this condition clearly, and for the student it falls comfortably into place beside such old friends as anuria and anencephaly. It might be objected that anhydramnios could be confused with the familiar term hydramnios. The latter, however, is a misnomer which should be scrapped. After all, hydramnios is merely the Greek for liquor amnii (liquor=*ὕδωρ*, amnion=*ἀμνίον*, and liquor amnii=*ὑδράμνιος*). An excess of liquor should always be called polyhydramnios.

I first became interested in anhydramnios after the birth of a stillborn daughter to a patient of mine who is also a personal friend. The tragedy was the greater because it was entirely unexpected. The patient, Mrs. N.K., primigravida, aged 23, had been well throughout pregnancy. She had proved most cooperative during her antenatal training and there appeared to be no obstetric abnormality. Her estimated date of confinement was 21st September, 1953. Clinically, she was at term on this date. It was not until 2 weeks later, on the 5th October, that labour began spontaneously at 6 p.m. with mild contractions. The foetus was in the L.O.A. position with head fixed and heart heard at normal rate and rhythm. By 8 a.m., on 6th October, the presenting part was one-third through, and the contractions were adequate in strength and recurring at 5-minute intervals. As the day wore on labour appeared to proceed normally. But by 5 p.m. the contractions, which were very strong, had become irregular, the intervals between them varying from 1 to 7 minutes. The foetal heart rate was normal. The cervix, though well applied to the presenting part, was only one-fifth dilated. Pethidine mg. 100 was administered at this time and was repeated at 8 p.m. At 9.30 p.m. no foetal heart sounds could be heard. The cervix was two-fifths dilated and well applied to the foetal skull. The patient was given morphine gr. $\frac{1}{4}$ and she then slept between contractions. Four hours later it became necessary to repeat the morphine. At 5 a.m., on 7th October, the contractions were again very strong and irregular. Labour had now been in progress for 35 hours and had been well established for 21 hours. The patient's general condition, however, was good and her morale had been excellent throughout. But, in spite of strong contractions, there had been no further descent of the presenting part, and the cervix was still only two-fifths dilated. Pethidine mg. 100 was given. Four hours later the contractions were again very strong, the lower segment was ballooning, and there was a marked Bandl's ring above it. There was no further cervical dilatation. It was decided that, notwithstanding the absence of foetal heart sounds, Caesarean section was necessary in the interests of the mother. When, at operation, a large thin-walled lower segment was incised, a small amount of glutinous green material escaped. The foetus weighing 6 pounds was delivered easily. The thick upper segment, which was sharply demarcated from the lower segment

* Read at the Fourth Annual Congress of the South African Society of Obstetricians and Gynaecologists.

and about half its size, contained no fluid whatsoever.

It is to be noted that the membranes had not ruptured either before or during labour, and at no time had any leaking of liquor been detected.

It seemed probable that the incoordinate uterine action and the death of the foetus had resulted directly from anhydramnios. However, on turning to the literature for confirmation, no description of this condition could be found, though there was an occasional brief reference to oligohydramnios. The latter was evidently considered to be of little moment, and most authors suggested no treatment. But Strachan (1947) advises that "the effect of a sedative followed, if necessary, by a uterine stimulant should be tried". Eden and Holland (1948) state that with oligohydramnios "foetal distress is liable to appear at any time during the first and second stages of labour". Others draw attention to the possibility of slow dilatation and painful contractions, but mostly the condition is dismissed as being of little significance. It was determined, therefore, to see whether the medical records of the Cape Town Teaching Hospitals would throw any light on the problem. I have thought for some time that labour may be initiated by the absorption of liquor amnii, and that the pound or two loss in weight which is frequently observed at the end of pregnancy is due to this fairly rapid extraction of liquor from the amniotic sac. It seems possible that, if pregnancy is prolonged and this absorptive process continues, there will be a danger of oligohydramnios and eventually anhydramnios. An irritable uterus and foetal anoxia could be expected as logical sequelae. The records of the last 4,000 consecutive deliveries at the Peninsula Maternity Hospital were examined. All cases of postmaturity (over 40 weeks), of prolonged labour due to incoordinate uterine action, of surgical induction of labour, and of foetal loss (cause unknown) were extracted. It was no surprise to find that the volume of liquor amnii was seldom recorded. Of the 4,000 cases there were 3 with the following 4 features in common:

(1) A loss of weight of 1 pound or more at or near term.
(2) The subsequent discovery of anhydramnios during attempted induction of labour for postmaturity (in 2 cases it is recorded that scalp hair was removed to confirm the absence of liquor).
(3) Prolonged incoordinate labour; and
(4) Foetal distress (necessitating the use of intrapartum oxygen in 2 cases, and resulting in neonatal death in the third).

These 3 cases exemplify what may be called the anhydramnios syndrome, viz.: prolongation of pregnancy after the "maturity" loss of weight, absence of liquor amnii at the onset of labour, incoordinate uterine action, and foetal distress. In the records examined there were many cases presenting some but not all of the above features, and in particular there were several where the presence or absence of liquor amnii had not been noted, though the clinical picture strongly suggested anhydramnios.

While I was working on these records James Walker's (1954) Blair-Bell lecture on foetal anoxia was published. In discussing the dangers of postmaturity he mentions what he describes as an extreme case. This was a primigravida aged 35 who had had a normal pregnancy. She gained weight steadily up to the 40th week and then lost a total of 6 pounds in the ensuing 4 weeks. An elective Caesarean section was performed at the 44th week (the reasons for doing so were not detailed) and "at operation no liquor was found". The child was covered with a thick layer of meconium. It was resuscitated with difficulty, but, in spite of expert treatment, died 15 hours later.

It appears to be established that anhydramnios, though it occurs rarely, is an obstetrical entity.

Treatment

In a case of postmaturity, particularly if there has been a drop in weight, the possibility of anhydramnios should always be borne in mind. (It is to be noted, however, that the "maturity" weight loss may be cloaked by pre-eclamptic toxaemia. Furthermore, if the liquor volume drops slowly, then a weight loss may not be evident.) When inducing labour on account of postmaturity, the Drew-Smythe catheter should be used, so that the amount of liquor present can be assessed with reasonable accuracy. Should

anhydramnios be diagnosed, incoordinate uterine action and foetal distress can be expected. Sedatives should be tried, though they seldom effect any permanent improvement in the character of an incoordinate labour. The use of oxytocics in these circumstances has obvious dangers. A close check must be kept on the rate and quality of the foetal heart. If the labour is short the risk to the foetus is probably not great. However, to allow the prolongation of an incoordinate labour where anhydramnios has been diagnosed, is to court disaster, for the foetal heart can stop without warning in such cases. It seems to me, therefore, that the rational treatment of anhydramnios is to allow a short trial of labour under close supervision, but to deliver by Caesarean section as soon as it is judged that the prospects of an early vaginal birth are poor.

Discussion

The volume of the liquor amnii in late pregnancy appears to be of more importance than we have hitherto realized. Harrison and Malpas (1953) have shown that in early pregnancy the function of the liquor is to provide an orderly and progressive distension stimulus, and so to maintain an isometric intra-uterine pressure. If, for any reason, the volume of liquor falls, the uterus becomes irritable and abortion ensues. Does not the same principle hold good for late pregnancy? Baird, Walker and Thomson (1954) have shown that the foetal death rate in the group "mature (cause unknown)" rises when pregnancy goes past term. They note that this phenomenon appears to be associated with defective foetal oxygenation and a relatively high incidence of difficult labour. May not these complications be due in some cases to anhydramnios, and in others to varying degrees of oligohydramnios?

These questions could be answered if liquor volume were routinely recorded in cases of surgical induction and at all births.

Postscript

Since this paper was read, Mrs. N.K., has been delivered of a live male infant by Caesarean section at term. The amniotic sac contained about 2 ounces of liquor. The baby had a left talipes equino-varus which is responding to treatment.

Summary

The addition of the word anhydramnios to the medical vocabulary is advocated. A case of anhydramnios is described. The significance of anhydramnios (and of varying degrees of oligohydramnios) as a cause of foetal and maternal distress cannot be properly assessed unless liquor volume is recorded routinely.

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FOETAL ELECTROENCEPHALOGRAPHY

BY

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PRELIMINARY studies have demonstrated by direct means the existence of brain activity in human foetuses of various ages (Okomoto and Kirikae, 1951a, b; Borkowski and Bernstine, 1955). This activity has been recorded in foetuses as early as 42 days of age (gestation) (Borkowski and Bernstine, 1955). Correlative studies have demonstrated electroencephalograms of foetuses *in utero*. These studies have been conducted successfully only in the last trimester of pregnancy. Thirty-two cases were reported in the previous study (Bernstine and Borkowski, 1955). No attempt was made to analyze or comment on the results obtained. In the present series, 25 cases are reported. The use of a new vaginal "electrode" is described and preliminary comment is made on the entire series of patients studied.

Procedure. The technique as previously described was used with few modifications. Bimanual examination under sterile precautions was done by one of the authors on all patients. The patient was catheterized as a routine procedure. Then the vaginal speculum electrode was inserted into the vagina. Visualization of the cervix and, in some instances (labour), of the foetal head was performed. More accurate placing of the electrodes was possible with this instrument than with the instrument in prior use.

The patient was now placed in a comfortable semi-reclining position and the electrodes were placed on the abdomen. All electrodes were connected to a standard eight lead Grass electroencephalograph machine. Readings were chiefly bipolar, but monopolar readings were also obtained. All patients were instructed to hyperventilate for 3 minutes at the conclusion of the recording.

Instrument. The instrument was modelled after the Graves vaginal speculum. It was constructed of lucite plastic which was shaped accordingly. Through each blade of the speculum channels were drilled to permit the insertion of the electrode wires. These electrodes were made of solid silver wire with a tip of silver solder over a copper bead. The electrode wires were insulated with rubber on their exit from the speculum so that they would not be in contact with the skin of the vulva.

Results. The findings of the 25 patients tested are presented in Table I. The results of the abdominal and vaginal electrodes are noted individually. Both types of testing were used on each patient. Although recordings were taken for periods of 20 to 40 minutes on each patient, the foetal electroencephalogram was evident for only part of the total time of the tracing.

Abdominal. In 10 of the 25 patients tested, foetal electroencephalogram was recorded.

Vaginal. In 21 of the 25 patients tested, foetal electroencephalogram was recorded.

In the present series, the low percentage of positive tracings obtained from the abdominal electrodes is attributable in part to the selection of cases in which the foetal head was in the pelvis (in certain cases, quite deeply in the pelvis). Thus the foetal head was below the symphysis pubis and not in close proximity to the abdominal electrodes.

TABLE I

Patient	Age	Race	Gravida	Para	Weeks of Pregnancy	Complications of Pregnancy	Condition of Baby (Birth)	Results
E.R.	31	W	11	8	Term	False labour	Good	*Abd.*—waves at 7/sec. of moderate voltage. *Vaginals*—waves at 7/sec. of moderate voltage. *HV*—no change.
E.R.	31	W	11	8	Term 2 days later	False labour	Good	*Abd.*—none observed. *Vaginals*—waves at 6 to 7/sec. of moderate voltage. *HV*—no change.
I.K.	23	N	2	1	33	Increase in FHS, moderately severe pre-eclampsia	Stillborn	*Abd.*—none observed. *Vaginals*—none observed.
I.K.	23	N	2	1	34	No FHS, pre-eclampsia improving	Stillborn	*Abd.*—none observed. *Vaginals*—none observed.
V.H.	34	N	5	2	Term	None	Good	*Abd.*—none observed. *Vaginals*—none observed.
S.L.M.	26	N	2	1	Term	Old healed pulmonary tuberculosis, false labour, external cephalic version 3 months prior	Good	*Abd.*—slow waves 1/sec. of moderate voltage with superimposed small waves at 7/sec. *Vaginals*—low voltage waves at 8/sec. *HV*—slowing to 4, 5/sec. *After HV*—return to previous rhythm.
A.G.	17	N	2	0	Term	Ruptured membranes, old healed rheumatic fever	Good	*Abd.*—none observed. *Vaginals*—waves of moderate voltage at 2 to 4/sec. *HV*—excellent build-up in voltage of waves of 2 to 3/sec. *After HV*—slow waves continue at previous voltage.
S.S.	17	N	1	0	38	In early labour	Good	*Abd.*—none observed. *Vaginals*—low voltage 7/sec. *HV*—no change.
E.C.	26	N	8	7	Term	Ruptured membranes	Good	*Abd.*—none observed. *Vaginals*—moderate voltage waves at 2 to 3/sec. with superimposed small waves at 7/sec. *HV*—slight build-up. *After HV*—return to previous rhythm and voltage.
G.M.	36	W	5	4	36	Pyelitis of pregnancy	Good	*Abd.*—low voltage 5/sec. *Vaginals*—low voltage 5/sec. 2/sec. with superimposed fast small waves. *HV*—no change.
N.L.L.	23	N	4	3	36	Mild pre-eclampsia	Good	*Abd.*—none observed. *Vaginals*—waves at 4 to 5/sec. of moderate voltage. *HV*—no change.
N.L.L.	23	N	4	3	Term	Mild pre-eclampsia, active labour	Good	*Abd.*—none observed. *Vaginals*—4½ to 6½ /sec. with superimposed fast small activity. *HV*—not done.
A.W.	23	W	1	0	Term	Rh negative, no titre	Good	*Abd.*—none observed. *Vaginals*—5 to 6/sec. *HV*—18/sec. *After HV*—return to previous rhythm and frequency.
A.W.	23	W	1	0	44	Rh negative, titre 1:1	Good	*Abd.*—low voltage 6/sec. *Vaginals*—4 to 7/sec. low to moderate voltage. *HV*—no change.
L.A.	40	N	6	5	36	Essential hypertension	Good	*Abd.*—6/sec. *Vaginals*—6 to 7/sec. *HV*—no change.
S.D.	20	N	1	0	Term	None	Good Premature 5 pounds 3 ounces	*Abd.*—none observed. *Vaginals*—5/sec. *HV*—no change.
C.R.	32	N	1	0	Term	In early labour	Good	*Abd.*—none observed. *Vaginals*—18/sec. *HV*—more apparent. *After HV*—still present—not as prominent.
A.C.	24	N	2	0	Term	None	Good	*Abd.*—none observed. *Vaginals*—5/sec. *HV*—no change.
E.D.	34	W	6	5	Term	In early labour, ruptured membranes	Good	*Abd.*—9/sec. *Vaginals*—12/sec., 18/sec. *HV*—4/sec. with superimposed fast small activity. *After HV*—no change.

HV=Hyperventilation.

TABLE I—*Continued*

Patient	Age	Race	Gravida	Para	Weeks of Pregnancy	Complications of Pregnancy	Condition of Baby (Birth)	Results
K.D.	19	W	2	1	Term	Epilepsy	Good	*Abd.*—10/sec. *Vaginals*—15 to 17/sec. *HV*—18/sec. more prominent. *After HV*—continuation of *HV* activity.
E.B.	23	N	5	3	Term	None	Good	*Abd.*—6/sec. *Vaginals*—6/sec. *HV*—no change.
F.D.	34	N	6	3	44	No FHS heard, cervix open 2 to 3 cm.: electrodes on head	Stillborn	*Abd.*—6/sec. *Vaginals*—6/sec. *HV*—build-up with appearance of high voltage (60 mm.) waves (anoxia??). *After HV*—slow return to previous activity.
F.D.	34	N	6	3	44	1 day before delivery, on foetal head	Stillborn	*Abd.*—none observed. *Vaginals*—none observed.
R.H.	26	N	1	0	Term	In active labour	Good	*Abd.*—small fast waves at 18/sec. *Vaginals*—small fast waves at 18/sec. *HV*—no change; fast activity continues. *After HV*—no change.
C.O.	21	N	3	2	36	Essential hypertension, grade 2 eye-grounds	Good (Caesarean section)	*Abd.*—no waves observed. *Vaginals*—waves of moderate voltage at 5 to 8/sec. slow waves of moderate voltage with superimposed small waves at 8/sec. *HV*—build-up of waves at 2 to 4/sec. of moderate voltage. *After HV*—persistence of above waves with slowing to 1 to 2/sec.

HV = Hyperventilation.

There were two stillborns (I.K., F.D.) in the present series. Both cases will be commented on fully in the discussion. In one instance (V.H.) the failure to record foetal electroencephalogram may be attributed to faulty technique in insertion of the vaginal speculum. The vaginal electrodes were placed deeply beyond the presenting foetal head.

Included in the present series are 2 pregnancies (four tests) which subsequently terminated in the delivery of a stillborn foetus.

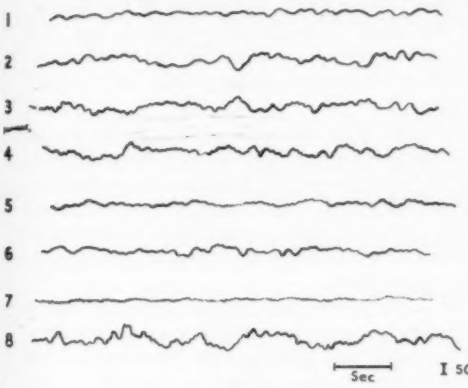

FIG. 1

Recordings from Vaginal Electrodes.

Foetal electroencephalogram; various types of rhythm; normal response to hyperventilation.

Vaginals.

1 to 6 Rhythm 5 to 8 per second; moderate voltage (C.O.)

7 Rhythm 18 per second; low voltage (R.H.)

8 Effect of hyperventilation (3 minutes) of mother on foetal electroencephalogram build-up of voltage (C.O.). 2nd Series.

Case F.D. was 34 years old, a negro, gravida-6, para-3, and 4 weeks past the expected date of delivery.

At the time of the first test no foetal heart sounds had been heard for a period of 3 days, whereas previously they had been audible. The mother had not perceived foetal movement for 2 days. Vaginal examination revealed the cervix to be open 2 to 3 cm. and the head at −1 to 0 station. The vaginal electrodes (anterior) were applied under direct vision upon the head of the foetus. Foetal electrocardiogram was absent. Foetal electroencephalogram revealed small waves at 6 per second from both vaginal and abdominal leads. Hyperventilation of the mother for 3 minutes produced a pronounced build-up in voltage (60 microvolts) (Figure 2). Similar waves had been observed in young foetuses by direct electroencephalography. They were believed to be the result of severe degree of anoxia.

Two and one-half days later, the test was repeated. At this time vaginal examination revealed a presenting head which was soft and flabby. Spalding's sign was positive. No foetal electrocardiogram or electroencephalogram was observed.

The next day a macerated stillborn foetus was delivered spontaneously.

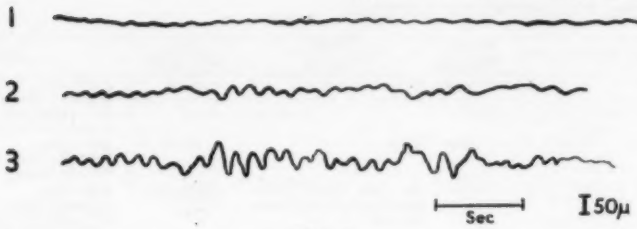

FIG. 2
Recordings from Vaginal Electrodes.
Case F.D. Foetal electroencephalogram; abnormal response to hyperventilation.
Vaginals.
1 Rhythm 5 per second; low voltage (F.D.).
Hyperventilation.
2 Rhythm 6 per second; moderate build-up (F.D.).
3 Rhythm 3 per second; very great build-up (F.D.).
2nd Series.

Case I.K. was 23 years old, a negro, gravida-2 and para-1.

This patient was a moderately severe pre-eclamptic under medical treatment. She responded temporarily then improved dramatically with the succumbing of the foetus and subsequent expulsion. The foetal heart rate had increased to 180 and had become irregular when the first test was performed (34-weeks of gestation). Foetal electrocardiogram was in evidence; foetal electroencephalogram was not obtained.

This woman was quite obese and the foetal head was high at the time of the tests. It was felt that this combination contributed to the failure in this case.

The second test was performed one week later at which time heart sounds were not heard, foetal movement was not perceived. Neither foetal electrocardiogram nor foetal electroencephalogram was observed.

A macerated stillborn foetus was delivered spontaneously 3 days later.

DISCUSSION

The electroencephalogram of the newborn infant has been studied recently in detail. Sureau, Fischgold and Capdevielle (1949, 1950) describe the principal frequencies of the brain waves from newborn as ranging from 1 to 14 cycles per second. Our studies are in agreement with these findings with a few exceptions. Occasionally frequencies of from 15 to 22 per second have been observed. We have seen these fast waves not only in the newborn, but in the foetus *in utero*. In some instances correlation (persistence of fast activity) between prenatal and postnatal tracings has been possible. Table II summarizes the patients in whom the fast waves have been observed prenatally. The incidence of fast brain wave activity in the cases studied is 15·7 per cent (9 of 57).

The cases presented in the previous paper and in this report allow certain preliminary conclusions.

It has been demonstrated that it is possible to record the electroencephalogram of the foetus *in utero*. According to the degree of the descent of the head (cephalic presentation) into the pelvis, recordings are obtained more efficiently utilizing abdominal (suprapubic) or vaginal leads.

Most of the cases studied (84·3 per cent) have a cerebral rhythm of from ½ to 14 cycles/second. In 15·7 per cent of the foetuses, faster rhythms (15 to 22 c/s.) (Figure 1) have been observed. This correlates with the incidence of abnormal electroencephalograms observed in the population as a whole.

In one instance, high voltage rhythm was seen in response to hyperventilation of the mother. This foetus was subsequently born dead. This type of high voltage waves was observed in two young foetuses (43 and 75 days) who were in "the process of dying". Similar observations were seen in 2 anencephalic newborns "who were dying". Whether or not this is pathognomonic of anoxia in foetuses awaits further studies.

The technique warrants further refinement and the value of the procedure as an indicator of foetal anoxia awaits more extensive study.

This procedure to be of value relies on the

TABLE II

Patient	Age	Race	Gravida	Para	Weeks of Pregnancy	Complications of Pregnancy	Condition of Baby (Birth)	Results
M.T.	20	N	4	3	Term	Epilepsy	Good	*Abd.*—low voltage slow waves at 3/sec. with superimposed fast waves at 22/sec.
F.C.	29	W	3	2	36	None	Good	*Abd.*—low voltage slow waves at 3/sec. with superimposed fast waves at 20/sec. build-up of activity with hyperventilation.
B.K.	20	N	4	2	44	Essential hypertension	Good	*Abd.*—low voltage slow waves at 3/sec. with superimposed fast waves at 20/sec.
F.F.	17	W	1	0	38	Pre-eclampsia	Good	*Abd.*—low voltage fast waves at 22/sec.
R.H.	26	N	1	0	Term	In active labour	Good	*Abd.*—small fast waves at 18/sec. *Vaginals*—small fast waves at 18/sec. *HV*—no change; fast activity continues. *After HV*—no change.
A.W.	23	W	1	0	Term	Rh negative, no titre	Good	*Abd.*—none observed. *Vaginals*—5 to 6/sec. *HV*—18/sec. *After HV*—return to previous rhythm and frequency.
C.R.	32	N	1	0	Term	In early labour	Good	*Abd.*—none observed. *Vaginals*—18/sec. *HV*—more apparent. *After HV*—still present—not as prominent.
E.D.	34	W	6	5	Term	In early labour, ruptured membranes	Good	*Abd.*—9/sec. *Vaginals*—12/sec., 18/sec. *HV*—4/sec. with superimposed fast small activity. *After HV*—no change.
K.D.	19	W	2	1	Term	Epilepsy	Good	*Abd.*—10/sec. *Vaginals*—15 to 17/sec. *HV*—18/sec.—more prominent. *After HV*—continuation of *HV* activity.

HV = Hyperventilation.

experienced electroencephalographer who must interpret the tracings.

SUMMARY

(1) Twenty-five additional cases of foetal electroencephalograms are presented.

(2) Positive tracings were obtained in 40 per cent of patients using abdominal electrodes; and in 84 per cent of patients using vaginal electrodes.

(3) A new instrument is presented for use as vaginal electrodes in this test.

(4) Fast rhythm (15 to 22 c/s.) was observed in 15·7 per cent of the cases.

(5) An apparent anoxic response was observed in one foetus who subsequently was stillborn.

The authors acknowledge the assistance of Doctor A. H. Price in construction of the vaginal speculum.

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SPINDLE CELL SARCOMA OF THE VAGINA

A Case Treated by Radium Implant

BY

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AND

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SARCOMA of the adult vagina is a rare disease. The tumour may be of the round cell, mixed or spindle cell type but the last is perhaps commonest.

CASE REPORT

The patient was a fit woman of 56. The menarche occurred at 14½ and the menopause took place suddenly 10 years before she came under observation. The cycle had always been 5/28, and she had produced 3 normal children.

For many years she had suffered from prolapse of the anterior wall of the vagina and a deficient perineum. In January, 1953, an anterior colporrhaphy and colpoperineorrhaphy were performed. A minor thrombosis occurred in the right leg during convalescence but this subsided uneventfully.

About one month later slight but persistent vaginal bleeding started. The patient was found to have developed a peculiar hard and nodular plaque in the anterior wall of the vagina. A tentative diagnosis of neoplasm of the vagina was made and biopsy was performed.

The section showed a spindle cell sarcoma, probably of muscular origin. There was very little collagen present, mitoses were frequent and there was considerable inflammatory infiltration (Figs. 1 and 2).

Examination under anaesthesia revealed an indurated mass in the anterior wall of the vagina situated about 4 cm. from the introitus. It extended upwards for about 5 cm., measured 2·5 cm. transversely and was estimated to be 1·5 cm. thick. It seemed quite mobile, but from its position and extent the urethra was almost certainly involved. The uterus was mobile, anteverted and not enlarged and there was no other abnormality in the pelvis. Cystoscopy was normal apart from a mild degree of cystitis.

There was no clinical abnormality elsewhere in the body and no significantly enlarged lymph nodes were palpable. All other investigations were also normal, and it was decided to treat the lesion with a planned implant of radium needles.

Treatment

The anterior wall of the vagina was treated as part of the surface of a cylinder. With a self-retaining catheter in position and the patient in the lithotomy position under general anaesthesia, five 2·0 mg. dumbell radium needles were inserted. Each needle was 5·8 cm. long of which 4·5 cm. were active, and the use of dumbell needles (more heavily loaded distally) ensured that the least accessible part of the tumour would not be underdosed.

The needles were spaced less than 1 cm. apart and were inserted in the long axis of the vagina as parallel as possible and about 0·5 cm. deep to vaginal mucosa. The vagina was packed with one roll of flavine gauze, and a catheter left in the urethra.

A radiograph showed that 18·1 cm. of vagina had been effectively implanted, and, bearing the dimensions of the lesion in mind, this was thought to be satisfactory. However, there was some splaying out of the needles (Fig. 3) particularly in the central part of the area, and, though this is frequently seen after radium implants of tubular organs, it was thought wise not to risk underdosing any part of the lesion.

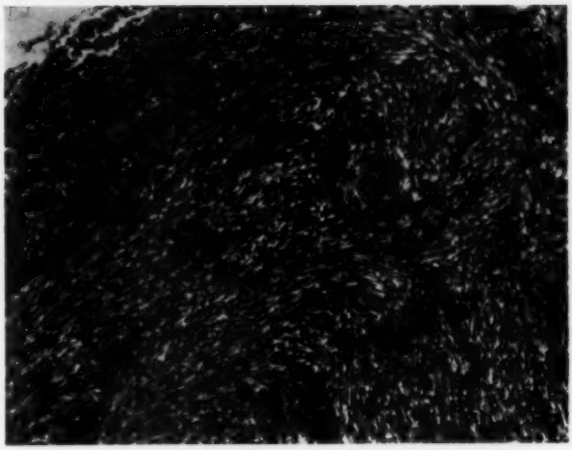

FIG. 1
Spindle cell sarcoma of vagina. ×50.

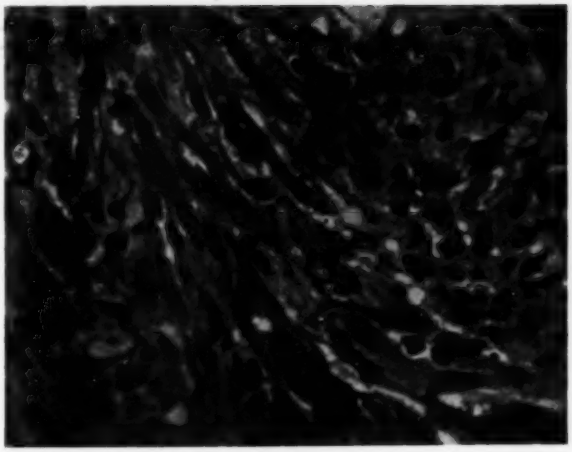

FIG. 2
Part of same field showing spindle cell structure with active mitoses. ×400.

FIG. 3
Radiographic appearances of radium implant of the vagina.

Therefore when the radium needles were removed under general anaesthesia 10 days later one 30 mg. radium ovoid was inserted into the most anterior and superior part of the vagina for 24 hours. The total dose given to the whole of the lesion from this combined treatment was 7,000 röntgens.

Progress

Recovery was uneventful. During the 6 months that followed considerable fibrosis developed. This improved steadily and the patient was left with a horseshoe stricture of the vagina about 2 cm. thick. Thirty-two months after the original implant, the patient is very well and the degree of post-irradiation thickening is diminishing steadily. There is no clinical evidence of residual or recurrent disease.

Comment

Because of the nature and situation of the tumour, surgical treatment would have meant bilateral transplantation of the ureters as well as major excision. It was thought reasonable to attempt radical treatment on a local basis only, using radium, and so far the outcome has been very satisfactory. These tumours tend to recur quickly, if they are going to recur at all, and the fact that the patient has had no trouble for over 2½ years means that there is now a reasonable chance of permanent cure.

A NOTE ON PATENCY OF THE FALLOPIAN TUBES

BY

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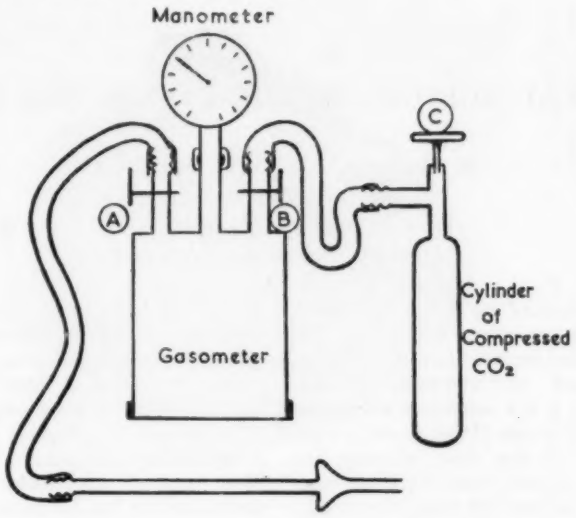
ON the last day of the recent Obstetrical and Gynaecological Congress in Oxford a series of well-organized papers on Hysterography and Salpingography was given. Not much attention, however, was given to the question of tubal function except determination of patency of the tube. Not infrequently one is confronted with a patient who brings a history of normal menstruation, whose husband is fertile and potent, who, on pelvic examination, possesses apparently normal uterus and appendages, who has had Rubin's test and a hystero-salpingography done and has been told that her tubes are patent. Yet she does not become pregnant. In my private practice I have had quite a few such patients, but as histories of these patients are 10,000 miles away I must rely on my memory for these notes. The apparatus I use for doing Rubin's test is different to the "hubble-bubble" type of apparatus in common use. I use an apparatus similar to the Douay apparatus I saw many years ago in France and which is made by Allen and Hanburys of London. It consists of a small metal gasometer of about 200 cm. capacity, soldered into the top of which are three short tubes on to one of which a manometer is screwed; the other two are fitted with taps and are connected by rubber tubing, one to the cervical cannula of standard type and the other to a small cylinder of compressed CO_2 with a regulating tap. In performing the test air is first driven out of the gasometer by filling with CO_2 under pressure and blowing out through the cervical cannula a couple of times. The cannula is then introduced into the cervix, tap A closed, gas up to a pressure of 80 mm. Hg let into the gasometer from the cylinder. Taps B and C turned off. Tap A is then turned on. The pressure immediately falls to about 60 due to filling of the uterine cavity (and perhaps also the tubes). I think this is due to a slight relaxation of the uterine musculature due to the pressure of the gas introduced, rather than a forcible distension of the uterus. If the tubes are patent and normal the pressure then slowly falls to 40 or 45 mm. Hg and the gas can be heard by stethoscope bubbling into the abdominal cavity. If, however, the tubes are patent but atonic, the pressure will *rapidly* fall to 20 or even 10, but I cannot remember any patient in whom the pressure has fallen below 10. If no gas escapes from the tubes, a series of trials is made with the pressure in the gasometer at various levels, 100, 120, 140, 160, 180 so long as the patient does not complain of any pain in the hypogastrium due to over-distension of the uterus. If there is stenosis of the tube or spasm, then at some pressure the gas will escape slowly from the tube and the pressure slowly fall, stabilizing at say 80 or even 100, but where spasm is extreme none will escape. As is well known, in the case where the fimbriated extremity of the tube is sealed by some filmy adhesions, it may unblock under pressure and gas escape, at first slowly and then more quickly and at subsequent tests at the same or lower pressure the pressure may finally come down to a normal or near-normal level of 40 or 50. In some patients the tubes may be found patent at say 100, the pressure falling to say 50, but at 160 no gas comes through and the pressure does not fall. I attribute this to a spasm of the tube secondary to increased pressure in the tube and I find that most of the patients described at the beginning of this note fall in this category. In these cases I recommend a nightly dose of bromide or phenobarbital. I believe that the excitement of the orgasm or anxiety for preg-



Not to scale

nancy causes a spasm of the tubes and maybe of the uterus and cervix too, for these patients often complain of post-coital hypogastric pain, which I think is due to uterine spasm. The dose of bromide or phenobarbital or a good alcoholic "binge" relaxes the spasm, the gates are open and the spermatozoa are able to make their way up the tube. In many of these patients pregnancy follows. One would like to know more of the mechanics of the passage of the fertilized ovum down the tube. Is it a slow onward progress or is the egg moved up and down sections of the tube by peristaltic and antiperistaltic movement in the tube, similar to what takes place in the lower bowel, until the changes take place in ovum and endometrium that determine embedding of the ovum? One would also like to know what part the cilia on the cells of the tubal lining play and whether this function is in any way co-ordinated with the function of the tubal musculature. Failure of the patient to have a baby may be due to failure or dysfunction of such a mechanism.

PATHOLOGICAL RUPTURE OF THE UTERUS DUE TO SARCOMA

BY

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SPONTANEOUS rupture of the uterus by tumour is a comparatively uncommon occurrence. The majority of the cases reported have been due to hydatidiform mole or chorionepithelioma, although there are a few references to rupture due to sarcoma. Williams (1894) found a total of 6 cases prior to that date, although the majority appear to have been found at post-mortem. Within the last 20 years Heyrowsky (1952) reported on a clinically symptomless myosarcoma perforating the uterus.

CASE REPORT

The patient, a married but nulliparous woman was referred to one of the gynaecological units of the Glasgow Royal Infirmary on 11th May, 1954 with a complaint of intermittent attacks of lower abdominal pain and difficulty with micturition.

The patient had reached the menopause in 1952 when she was 51 years of age and no further vaginal bleeding had occurred since that time. She complained of intermittent attacks of generalized lower abdominal pain which had troubled her for 5 months. Attacks of pain had occurred with increasing frequency in the last 3 weeks preceding her attendance at the hospital. She had also noticed a swelling of the lower abdomen, the appearance of which was coincidental with the onset of her abdominal discomfort. This swelling had progressively increased in size and had recently become rather tender. There had been no retention of urine, dysuria or frequency of micturition.

EXAMINATION FINDINGS

The lower abdomen was distended by a firm irregular mass apparently arising from the pelvis. The mass which extended from the symphysis pubis to the umbilicus was tender, irregular in outline and had attained approximately the same size as a pregnancy of 5-months duration. There was no evidence of ascites.

Vaginal examination confirmed the presence of an intrapelvic mass extending into the abdomen. The mass appeared to be an irregularly enlarged corpus uteri. No abnormality of the cervix was found. A little blood-stained fluid was found on the examining fingers.

In view of the irregular uterine enlargement a provisional diagnosis of multiple uterine fibromyomata was made and arrangements were made for her admission to the hospital for laparotomy.

On 18th May, 1954 the patient was referred to hospital for admission by her own doctor because of an acute exacerbation of the symptoms. The abdominal pain was now continuous and severe although variable in intensity. Slight vaginal bleeding had been present since her previous visit to the hospital. Her appetite had been poor and she felt nauseated although there had been no vomiting.

On examination a marked deterioration in the patient's general condition had occurred. She was pale, restless and obviously in severe pain. The pulse rate was 120/min. and the temperature 101° F. The blood pressure was 120/70 mm. Hg. Her general condition was assessed as "fair". Examination of her respiratory and cardiovascular systems revealed no gross abnormality.

Abdomen. The lower abdomen was now rigid and markedly tender. Tenderness above the umbilicus was also present but was less marked. The abdominal mass was still present although it was now much more difficult to palpate than formerly due to abdominal tenderness and rigidity. A dull note to percussion was obtained in both flanks and in the centre of the lower abdomen. Vaginal examination was difficult due to tenderness. The presence of a pelvic mass was

FIG. 1
In this photograph glass rods have been inserted into the cervix (A) and the site of rupture (B). The uterus is grossly distorted by the tumour.

FIG. 2
This shows a cut through the uterus and tumour. The uterine canal (A) can be seen running upwards near the posterior edge of the specimen. Areas of necrosis and haemorrhage are evident in the main tumour mass and the site of rupture is indicated at (B).

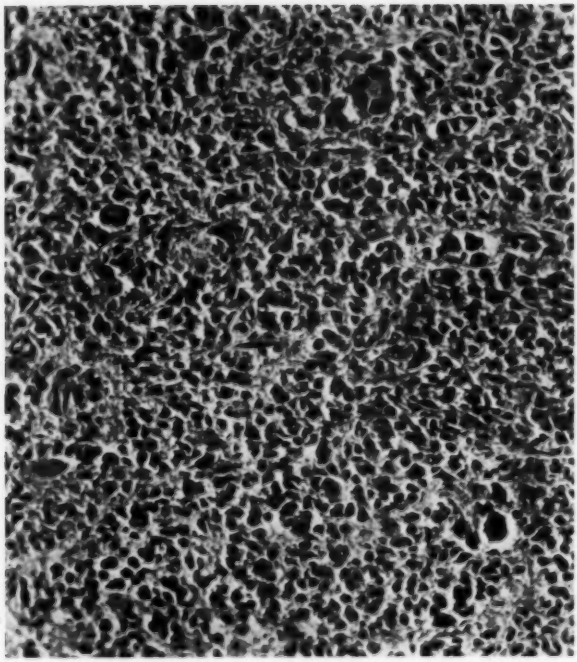

FIG. 3
Histologically the tumour is a typical mixed-cell sarcoma with occasional giant cells and many bizarre nuclei. H. & E. ×250.

again noted but rigidity of the abdominal musculature prevented accurate definition of its outline. Fullness of the pouch of Douglas was now noted. The cervix again presented no abnormality. Slight vaginal bleeding occurred during examination and this owed its origin to a small polypoidal swelling about the size of a small marble situated on the anterior vaginal wall just behind the urethral orifice. This polyp was reddish purple in colour and bled freely on palpation. It was a recent development as the vaginal canal had been inspected with negative results during the course of the previous examination.

Rectal examination revealed little of note. The rectal canal was ballooned but faecal material was present in the lower gut.

Other Investigations

Haemoglobin—10·0 grammes per cent.

Red blood cell count—3·7 million per cubic millimetre.

White blood cell count—30,000 per cubic millimetre.

Erythrocyte sedimentation rate—85 millimetres in the first hour.

The findings described were very suggestive of rupture of an abdominal viscus and the high white blood cell count and E.S.R. seemed to indicate that the rupture was associated with intra-peritoneal infection. After consultation with the surgical staff a provisional diagnosis of uterine malignancy in a fibroid uterus involving the bowel with secondary perforation and peritonitis was made.

At laparotomy about 1 pint of free blood was found in the peritoneal cavity. When this was removed the uterus was seen to be irregularly enlarged and distended by multiple uterine fibroids and presented a congested appearance. Rupture had occurred in a large intramural fibroid on the anterior uterine wall of the uterus and a large portion of friable tumour tissue brain-like in consistency about four inches in diameter was found lying free in the utero-vesical pouch. The rupture admitted two fingers and communicated with both uterine and peritoneal cavities. The uterine wall in the region of the perforation was friable and infiltrated with tumour tissue. The omentum was adherent to the superior margin of the rupture in the uterus and adhesions between the posterior wall of the uterus and the pelvic colon were also present. Low subtotal hysterectomy was performed as a palliative measure since spread of malignancy beyond the confines of the uterus had already occurred. The abdomen was then closed and the blood transfusion which had been given throughout the operation was discontinued.

After operation her general condition improved markedly. Fourteen days later excision of the small tumour growth on the anterior vaginal wall was carried out.

Pathology

Uterus. The uterus was enlarged and distorted by multiple intramural fibroids. A large tumour 4 inches in diameter situated on the anterior wall had ruptured on the peritoneal surface, the rent extending inward to the uterine cavity (Fig. 1). This tumour was very soft and friable and on section presented many soft yellowish areas and much hyalinization (Fig. 2).

The portion of tumour tissue recovered from the abdominal cavity weighed 170 grammes.

Histology

The tumour was found to be a mixed cell sarcoma (Fig. 3), widely infiltrating the uterine wall and extending to just above the line of excision in the cervix. It is possible that the growth originated in the largest fibromyoma, but there was no convincing histological evidence to substantiate this. The material from the abdominal cavity consisted entirely of sarcomatous tissue. The endometrium was found to be atrophic.

Histological examination of the vaginal polypus was also carried out. The tissue proved to be a mixed cell sarcoma showing a histological pattern similar to that in the uterine tumour.

Subsequent History

One month after operation a palliative course of X-ray therapy was commenced but on account of nausea, vomiting and constitutional disturbances this treatment was stopped after the tenth exposure. A short period of clinical improvement occurred after cessation of X-ray

therapy but one week later the patient had an irregular pyrexia and progressive deterioration of her general condition became evident. She developed increasing dyspnoea associated with slight cyanosis. Signs of patchy consolidation affecting both lungs were found on 4th August and this was confirmed on radiological examination of the chest, the appearances being suggestive of secondary tumour deposits in the lungs. Further deterioration occurred and the patient died on 10th August.

Post-mortem Findings

At autopsy the abdominal cavity was remarkably free of tumour deposits. One small secondary tumour was found in the right lobe of the liver. There was evidence of fibrosis in the pelvic operation site and numerous peritoneal adhesions had formed but no sarcomatous deposits were found. The uterine veins were identified and found to be full of organizing thrombus which extended into both internal iliac veins but no sarcomatous tissue was present.

Both Fallopian tubes and ovaries showed no abnormality on macroscopic and histological examination. The cervical stump which measured one inch in length had also escaped sarcomatous infiltration. The remaining pelvic and abdominal organs presented no abnormality.

Both lungs were partly collapsed and contained innumerable secondary tumour deposits, many of which projected from the pleural surface. The largest single tumour measured approximately 3 inches in diameter. Several hilar glands had been infiltrated by the growth. A moderate pleural effusion was present on both sides. The histological pattern of the pulmonary tumours was in all respects similar to the original uterine growth.

Apart from an atheromatous condition of the coronary arteries no gross abnormality was found in the other organs.

Summary

A case of pathological rupture of the uterus by sarcoma is described. The main features of interest are (1) that a provisional diagnosis of uterine sarcoma could be made, assisted by the presence of the small tumour on the vaginal wall, (2) the similarity to an acute infection in the abdomen (leucocytosis, high erythrocyte sedimentation rate and the degree of pyrexia), and (3) the complete absence of any evidence of local malignant spread of the tumour in the abdomen three months after operation.

We wish to express our thanks to Dr. Hugh Stirling for permission to publish the case and to Professor Symington's staff for their assistance in preparing and photographing the specimens.

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INTRA-UTERINE SEPARATION OF THE UMBILICAL CORD

BY

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SEPARATION or rupture of the umbilical cord before birth is a rare event. It may occur as a complication of internal version or of labour, and in such cases may be associated with an abnormally short cord, a malformed foetus (Bancroft-Livingston, 1948), prolapsed cord (Sackett, 1934) or with a velamentous insertion of the cord lying in front of the presenting part (Kirwan, 1947). Intra-uterine separation of the cord, not apparently associated with labour, is seldom reported. McClintock (1943) could find no previous case recorded in Great Britain, although she quoted several instances from the American literature. The present case of intra-uterine separation of the umbilical cord is described purely for its academic interest as diagnosis and treatment are, at present, impossible.

CASE REPORT

The patient is 33 years old. The blood is Rh positive and the Wassermann reaction is negative.

Previous Obstetric History. She was married in June, 1951. She had an abortion at 12 weeks in October, 1951. In February, 1953 she had a normal female child by Caesarean section, after being 4 days in labour with primary uterine inertia. In May, 1954 she had a miscarriage at 28 weeks, the foetus having been dead for about 6 weeks. Labour started as an accidental haemorrhage.

Present Obstetric History. The last menstrual period commenced on 30th June, 1954. The patient was seen at monthly intervals from the 10th week. The urine and blood pressure were normal. The haemoglobin was 65 per cent (Sahli). She was treated for 4 months with oral ferrous gluconate without response. Twenty c.cm. of an intramuscular iron preparation (Imferon) were given and in 4 weeks the haemoglobin level had risen to 70 per cent (Sahli) and remained at this level till after confinement. The patient's improved general condition and feeling of well-being were out of all proportion to the small rise in the haemoglobin level.

The patient was most apprehensive about her confinement as a result of the previous intra-uterine death. She did not feel life on 5th February, 1955, but when examined the foetal heart was heard. On 6th February the foetal movements were felt, but on the following day they were feeble and then ceased. No foetal heart was heard on 7th February. An X-ray on 12th February showed a single foetus with a vertex presentation but no evidence of intra-uterine death was noted. The patient did not attend for further X-rays. Labour commenced on 9th March, i.e., at 36 weeks, and after 4 hours the foetus was delivered as an extended breech. After delivery of the body it was noted that there was no cord attached to the umbilicus, the stump was sealed off rather like the normal appearance on the 7th postnatal day. The liquor was port-wine coloured as if stained with blood. The placenta came away immediately after delivery of the head. There was a normal puerperium during which the haemoglobin rose to 80 per cent (Sahli) without further treatment.

Pathology. The specimens are a macerated male foetus weighing 1,250 g. and measuring 28 cm. in crown–rump length, and a 225 g. placenta with membranes complete and a centrally inserted cord (Fig. 1). Protruding from the umbilical region of the foetus there is a tapering thread-like remnant of the umbilical cord. The free end of the placental portion of the cord is rounded, with a thin tapering tag at the extremity (Fig. 2). The umbilical cord shows no evidence of pathological torsion. Histological examination of the free end of the placental portion of the cord showed no specific features other than changes ascribed to maceration.

Discussion

In this case the factors leading to separation of the cord must have operated before the onset of labour because, while the attenuated portion of the cord at the umbilicus could easily have parted at any time after the death of the foetus, it is improbable that the anatomical features of rounded ends with a thread-like connexion at the site of separation could be produced by traumatic rupture of the cord during labour. Other possible mechanisms which require consideration are knotting and torsion of the cord.

Knotting of the cord is a rare cause of foetal distress or intra-uterine death, although a considerable number of cases have been recorded (Price, 1947; Peterson, 1952). We have been unable to find any case in which knotting of the cord has been followed by rupture. Torsion of the cord is discussed in detail by Browne (1925) who credits Ruysch with having first described the condition in 1691.

Browne in his article describes several umbilical cords which had undergone extreme torsion resulting in numerous twists along their length. However it often happens that the portion of cord near the umbilicus is alone affected, due perhaps to a lesser amount of Wharton's jelly or to an alteration in its physical properties at that point. This focal concentration of the effects of torsion may be readily reproduced if part of an umbilical cord is traumatized to reduce the turgor of Wharton's jelly at one point and the cord is then twisted upon itself. The case described by McClintock falls into this category; the cord was 24 inches in length and was torn ¼ inch from the umbilicus. It was described as being "normal except at the umbilical end, where it was swollen and looked rather sloughy".

As regards the causation of pathological torsion, Browne states that the condition is most common in multiparae, presumably because there are more opportunities for free foetal movements. Male foetuses are more often affected than females. Excessive movements and abnormal length of the cord are also mentioned.

Simpson in 1859 published an article on the "spiral direction of the umbilical vessels" in which he reviewed the various theories of pathological torsion. Velpeau asserted that twisting of the cord was due to the powers of rotation of the foetus, by means of limb movements, although admitting that this random process did not fully explain why the spiral is, in most cases, from left to right. Van der Kolk supposed the torsion to be due to the greater arterial pressure in the cord causing a recoil on the pelvis of the floating embryo according to whether the arteries are placed on the left or right side of the umbilical vein in the annulis umbilicalis.

Simpson pointed out that the aorta in the foetus lay on the left side of the vertebral column and that the right iliac artery was in a more direct line with the aorta and was of larger calibre than the left. He argued from this that the flow of blood was greater in the right and that at the umbilicus, where the two arteries converge and emerge one on each side of the umbilical vein, the recoil of the right vessel being greater tended to act more strongly on the foetus causing it to rotate. In support of his theory Simpson pointed out that torsion is not seen before the completion of the early development of the heart, that is before the eighth week, and that it becomes a more obvious feature as the force of the heart beat increases with the approach of term.

A moderate amount of torsion is physiological, few cords being free of twisting although the normal cord tends to recoil to an untwisted position. This resumption of a neutral position may readily be verified experimentally. It is more striking if the vessels are distended with blood or saline. This elastic recoil is largely due to the nature of normal Wharton's jelly which has a firm consistency when *in situ* and resists deformation. If this feature is lacking at one portion the effects of torsion will be concentrated at this area and constriction of the blood vessels may then occur with death of the foetus. The torsion may be such that, as in the case here reported, the cord becomes twisted off at the umbilicus. It appears probable that the basic cause is not torsion but rather the inability of an abnormal cord to resist it.

Summary

The clinical and pathological features of a case of intra-uterine separation of the umbilical cord with resulting foetal death are described.

FIG. 1
Foetus, placenta and cord, showing the site of separation of the cord.

FIG. 2
Enlarged view of the site of separation of the cord.

The condition is considered to result from torsion acting on an abnormal cord.

Acknowledgments

We should like to express our thanks to Professor C. H. G. Macafee and Professor J. H. Biggart for their interest and help in preparing this paper.

The photography is the work of Mr. D. Mehaffey, A.R.P.S.

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A CASE OF CHORIOANGIOMA

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IN our present state of knowledge chorioangioma can scarcely be regarded as a clinico-pathological curiosity, but for the fact that it is often complicated by hydramnios. Hydramnios, however, is frequently associated with congenital malformations. Cases of chorioangioma should be reported not only because of their rarity, but in order to obtain a sufficient number of cases which would ultimately allow of an analysis regarding the question of the co-existence of congenital malformations of the foetus.

The association of chorioangioma with hydramnios may also help to throw light on the question of the origin of liquor amnii.

CASE HISTORY

Mrs. B.E.K., a healthy primigravida, aged 24 years, booked for her confinement on 29th April, 1954, when she was 10-weeks pregnant. She gave no history of any previous illness of note with the exception of rubella in childhood. She attended regularly for antenatal care at the Cambridge Maternity Hospital. Her pregnancy advanced uneventfully, except for trichomonas vaginitis which responded to treatment.

Two days before delivery the clinical diagnosis of hydramnios was recorded. An X-ray film of the abdomen did not reveal any abnormality of the foetus. She had a normal delivery on 14th November, 1954 (i.e., 5 days before the expected date), after a labour lasting 5½ hours. The child, a female, weighed 5 pounds 15 ounces, was normal at birth and had not revealed any abnormality when seen 4 months after delivery.

The placenta was delivered after 15 minutes with a total blood loss of 12 ounces.

DESCRIPTION OF THE PLACENTA

Macroscopic (Fig. 1). The placenta was of the circumvallate type, of oval shape (20×14×4·5 cm. in diameter). The cord was inserted centrally. The membranes were ragged, but apparently complete. On the foetal surface, 3 cm. from the insertion of the cord, was a convex tumour (6×5 cm.), of a firm even consistency, covered by amnion. Branches of the umbilical vessels were running over it. The maternal surface was lobulated. The cut surface was purple-brown and there were a number of grey-white areas. The surface was divided up incompletely by fibrous strands.

Microscopic. The surface of the tumour was incompletely covered by a very thin layer of syncytium (Fig. 2) investing a layer of connective tissue fibres which were mainly arranged in wavy bands running parallel to the surface. Between these fibres were scattered, deeply stained, elongated nuclei. In most parts the epithelial covering was barely discernible. A number of large blood vessels were seen in the deeper layers of the connective tissue fibres and accompanied trabeculae which penetrated into the depth of the tumour.

The bulk of the tumour (Fig. 3) was made up of innumerable capillaries, in some parts packed closely together, with very little intervening stroma, whereas the stroma was more obvious in others. Some of the capillaries contained red blood corpuscles, many of them haemolysed. The capillaries were lined by typical endothelium. In some areas a lumen was only imperfectly developed and in these nuclei were more numerous.

DISCUSSION

Considering that chorionic tissue has normally a tendency to proliferate and to invade maternal tissues, it is surprising that neoplasms of the placenta are rare. There are three varieties of placental tumours. One involves the villus as a whole: hydatidiform mole; one consists of epithelium only: chorion-epithelioma; and one is made up of villous stroma: placental haemangioma or chorioangioma.

FIG. 1
Placenta Circumvallata with chorioangioma.

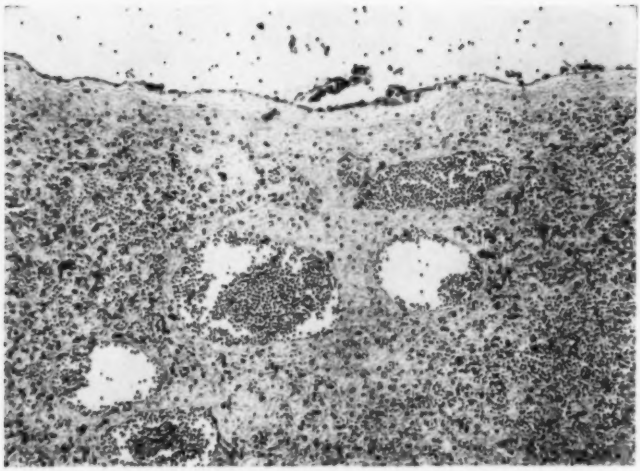

FIG. 2
Chorioangioma, showing thin surface layer of syncytium investing a layer of connective tissue. Between the capillary sinuses are 5 large blood vessels. ×75.

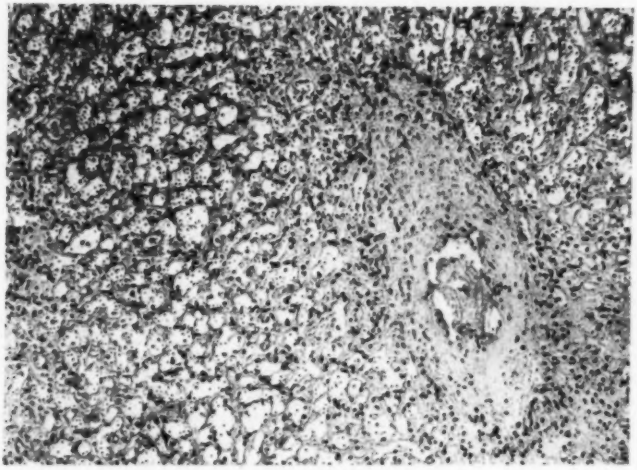

FIG. 3
Chorioangioma, showing innumerable capillaries packed closely together, with very little intervening stroma. ×90.

Nomenclature

The tumour has received a variety of different names, depending on the prevalent histological characteristics: myxoma fibrosum placentae (Virchow, 1867); myxo-fibroma (Goodhart, 1877); fibroma (Kramer, 1890; Bode and Schmorl, 1895); chorioangioma (Nebesky, 1914); chorio-angio-fibroma (Siddall, 1924). In recent papers the terms placental angioma and chorioangioma have been used.

Historical

There seems to be general agreement that the first authentic case was reported by John Clarke in 1798 in this country.

In Siddall's classical paper in 1924, 130 previously reported cases were reviewed, including one of his own. Kühnel, in 1933, brought the number of reported cases to 163, and Barry, McCoy and Callahan were able to bring the total up to 235 in 1951. Since 1951, one case has been added by Kendrick and Stofer (1952), one by Bury (1954) and another by McInroy and Kelsey (1954).

Incidence

Siddall (1926) reported that examination of 600 placentae by sectioning them into slices of between 5 and 8 mm. thick revealed the presence of a small chorioangioma in 6 cases. Some of the tumours were so small that they were only diagnosed histologically.

Leopold (1895) had found only one tumour in 7,000–8,000 placentae. Kühnel carried out a search in 500 placentae without finding a single case. They do not, however, describe their method of search in detail.

Thus it is quite possible that small tumours, particularly if situated within the placenta, may escape unnoticed and that chorioangioma is more common than one would assume from the number of published cases; but such small tumours are probably without clinical significance.

Naked Eye Appearance

The tumour is usually ovoid or hemispherical. Most reported tumours projected from the foetal surface of the placenta and were sessile, but some were situated within the depth of the placenta. Virchow (1863) and Fisher (1940) reported tumours situated on the maternal side; in one of Fisher's cases the tumours were pedunculated. In the series of 163 reviewed by Kühnel (1933) the tumour was in the marginal part of the placenta in 12 per cent of cases. In another 12 per cent it was separate from the placenta, connected to it merely by a cord containing blood vessels. The tumour reported by Barry, McCoy and Callahan (1951) arose from the umbilical cord; Emge (1927) attributed the tumour in his case to a similar origin. The foetal membranes usually cover the tumour.

In Siddall's series (1924) of 130 the size of the angiomata ranged from that of a minute nodule to a tumour weighing 780 g. Emge described a neoplasm as large as a "child's head".

In the reported cases the tumour was usually single, but occasionally multiple tumours have been described. Fisher (1940) reported a placenta containing 25 pedunculated chorioangiomata.

Most of the published tumours were of a dark bluish-red colour, but occasionally they varied from pale yellow to a mottled red.

The tumour tends to be firmer than the remainder of the placenta. By feeling the placenta between fingers and thumb, the palpable change of consistency may lead to the more frequent detection of small chorioangiomata. The firmer varieties approach the consistency of a fibroma. In Fisher's case (1940) the tumour was spongy and cystic.

On cross section the tumour is usually seen to be well-defined from the remainder of the placenta and can, as a rule, be easily enucleated. It is demarcated from the normal placental tissue by a pseudo-capsule caused by compression of adjacent villi (Siddall). Trabeculae divide the tumour incompletely on the cut surface. The colour of the cut surface may again be mottled bluish-red. The more cellular types of chorioangioma are said to be of a greyish-red colour, while the vascular types are a deep bluish-red (Roth, 1947).

The Appearance of the Placenta

The placenta in the case under review was of the circumvallate type (Fig. 1). Whitridge Williams (1927) believed that circumvallate

placenta develops when the chorionic plate, once formed, becomes too small for the requirements of the foetus. As a result the villi at the periphery can only increase the surface area of contact with maternal sinuses by growing out further from the periphery of the chorium frondosum, between the layers of the decidua, because the demarcation line between chorium frondosum and chorion laeve has by that time been established. This mode of development of placenta circumvallata had already been suggested by Robert Meyer in 1912.

Kühnel (1933) states that the placenta is often unusually heavy and large and suspects that the high foetal mortality in cases of large chorioangioma may be due to insufficient hyperplasia of the normal placental tissue. The circumvallate appearance of the placenta reported in the present case may be due to hyperplasia compensating for the non-functioning neoplasm in the placenta. No reference to placenta circumvallata has been found in the literature studied for this paper.

Histological Features of Chorioangioma

The variations in the nomenclature are the result of differences in the microscopic appearances observed by the various authors. In most cases the bulk of the tumour is made up of angiomatous tissue, that is, capillary spaces which either contain blood or haemolysed red cells, or are empty. Variations in the relative proportion of stroma and in the differentiation of capillaries from angioblastic precursors account for differences in the histological picture of the cases reported. Thus in Siddall's case (1924) fibrous tissue predominated. In one of Fisher's cases (1940) the tissue was partly angiomatous, partly fibrous and partly myxomatous. In his other case the tumours were mainly of the angiomatous type with little immature supporting stroma. Cases have been reported which were predominantly cellular, and others which showed degenerative changes (Marchetti, 1939). The peripheral connective tissue (Fig. 2) was mentioned also by Marchetti, and Davies (1948). Syncytium was commonly found as a rather incomplete superficial layer surrounding the tumour.

Origin

As the tumour, in the vast majority of reported cases, was situated on the foetal side of the placenta, it was thought that it had derived from proliferation of a villus which had failed to establish the normal relationship with the decidua. If one considers that there would be less resistance against the tumour bulging into the amniotic cavity, rather than into the uterine wall, the reason for the predominance on the foetal side may be purely mechanical. Benign tumours do not invade neighbouring tissues but rather displace them by their growth. Siddall (1924) thought that the tumour derives from a single villus. The 25 tumours in Fisher's second case (1940), each hanging on a delicate pedicle, would support this view.

In cases where tumours were situated some distance from the placenta, but connected to the umbilical cord by a leash of vessels, their situation may be explained in a similar way to that of a succenturiate cotyledon (Bode and Schmorl, 1895).

Albert (1898) suggests that the tumour might arise from vessels of the allantois, believing that the allantoic vessels normally give rise to the vessels of the chorion, and that if, for some unknown reason, a branch develops from the umbilical artery proximally and, covered with chorion, fails to reach its normal destination for further development, it proliferates in a disorderly neoplastic manner, thus producing a chorioangioma.

With regard to the histogenesis, Marchetti (1939) is convinced that the neoplasm originates from chorionic mesenchyme, presumably because he adheres to the view that the latter normally gives rise to the vasculo-connective tissue of the villus. Davies (1948) "impressed by the similarity of the cells and syncytial masses in the more vascular areas of the tumour to the parent tissue of all endothelium, the angioblastic tissue" suggests that the tumour might well originate from primitive angioblastic tissue taking on neoplastic tendencies.

Although the tumour always has vascular connexions with a branch of the umbilical vessels, even when it is situated some distance from the placenta, this does not prove that it develops as a bud from a branch of the umbilical

vessels. One has to keep in mind that villus vessels do not develop as outgrowths of umbilical vessels, but form *in situ* from multiple angioblastic foci in the primitive trophoblast (Hertig, 1935).

Clinical Features

All authors agree that there does not seem to be any relationship between the occurrence of chorioangioma and age or parity, nor do there seem to be any predisposing factors or associated diseases, or abnormalities, except hydramnios. While in the majority of the reports chorioangioma was without clinical significance, the following cases illustrate complications which may arise.

Roth (1947) described a case which presented with painless ante-partum haemorrhage at 37 weeks, attributed to low implantation. In Virchow's case (1863) premature labour followed severe ante-partum haemorrhage. In Sautner's case (1923) a tumour the size of a walnut had broken away from the placenta and had been retained leading to secondary post-partum haemorrhage on the 11th day of the puerperium. The tumour described by Bode and Schmorl (1895) had derived from a patient who had a stillbirth at 7 months, followed by a post-partum haemorrhage. The child had died *in utero* a few days previously. In Margeson's case (1920) a large tumour caused obstruction to delivery necessitating Caesarean section. In Emge's case (1927) a chorioangioma the size of a child's head caused difficulty in the second stage as the tumour was situated between the head and the anterior shoulder. There is a tendency for the baby to be born prematurely which may be due to hydramnios. The foetal and neonatal mortality is increased owing to prematurity and may sometimes be due to congenital malformations.

Hydramnios

Hydramnios seems to be relatively common in association with chorioangioma. Siddall (1924) reports it in 32·7 per cent of 110 cases for which data were available. Hydramnios was present in 90 per cent of large tumours, and the incidence of hydramnios in his series increased parallel with the size of the tumour. The tendency to hydramnios was confirmed by subsequent authors (Kühnel, 1933; Barry *et al.*, 1951). There was no history of hydramnios in Marchetti's 8 cases, but the tumours were small except one which measured $5 \times 6 \times 6$ cm.

The cases reported by Bury (1954) and by McInroy and Kelsey (1954) had severe hydramnios which was treated by paracentesis.

The cause of hydramnios is obscure. The association of chorioangioma with hydramnios might be regarded as an argument in favour of the view that the liquor amnii is of foetal origin. It may, however, have a composite origin; partly as a secretion of the amniotic epithelium, and partly as a transudate from the maternal blood. The foetus probably adds to the liquor by micturition. That the foetus swallows liquor *in utero* is shown by the presence of lanugo and epidermal squames in its intestine. The inspissated condition of the intestinal contents suggests that fluid is absorbed into the foetal circulation by which it is transported to the placenta where it takes part in the general exchange between the foetal and the maternal blood.

The amount of fluid in the amniotic cavity will depend on the balance between secretion and absorption. Obstruction at any point in the circuit may lead to damming up of fluid behind it and thereby cause hydramnios. On the other hand, fluid may accumulate owing to excessive secretion. Hydramnios could therefore be due to a variety of causes.

In the case of chorioangioma it may be due to circulatory obstruction by the tumour which is always supplied by a branch of the umbilical vessels.

Kotz and Kaufman (1939) attribute the hydramnios to transudation of fluid from the capillaries of the chorioangioma.

McInroy and Kelsey (1954) point out that the blood circulating through the tumour and returning through a tributary of the umbilical arteries to the foetus has not passed through the placenta and will therefore be in a "non-oxygenated and unimproved state", returning waste products to the foetus which should normally be removed by the placenta. This may call for increased renal activity and secretion of foetal urine.

It is common knowledge that hydramnios is frequently associated with malformations. Among the reported cases of chorioangioma there is very little information with regard to foetal abnormalities, particularly concerning the occurrence of malformations of the circulatory system and other haemangiomata in the foetus. One would have thought that the association of hydramnios with chorioangioma would have led to comments on a search for such malformations. These may have been masked partly by the fact that most children survived. However, autopsy carried out in the case described by Barry *et al.* (1951) showed "incomplete division of the truncus arteriosus with right aortic arch, and dilation of the heart, most advanced on the right; and cavernous hemangioma of the liver". In Merttens' case (1895) the stillborn mature child was oedematous and had stenosis of the isthmus of the aorta. In one of Kühnel's cases (1933) the umbilical cord contained only two vessels. Fisher (1940) mentions that in one of his cases the foetus suffered from anencephaly and spina bifida.

Summary

(1) A case of chorioangioma in a circumvallate placenta is described.

(2) An account is given of the naked-eye and histological appearances of this and other reported tumours.

(3) The clinical features are described briefly with special reference to hydramnios and its causation.

I wish to thank Dr. A. M. Barrett, of the University of Cambridge Department of Pathology, for helpful criticism and Mr. Oswald Lloyd for permission to publish the case.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of Council was held in the College House on Saturday, 24th March, 1956, with the President, Mr. Charles Read, in the Chair.

Professor Naguib Mahfouz will give the William Meredith Fletcher Shaw Memorial Lecture on 17th July on "Urinary fistulae in Women".

The President, Mr. C. D. Read will inaugurate the South African Regional Council of the College at Durban in July.

Mr. Humphrey Arthure has been appointed representative on the Central Council for District Nursing.

The Honorary Fellowship of the College is to be conferred on the Rt. Hon. The Viscount Nuffield and Lt.-Gen. Sir Ronald Weeks. A ceremony of admission will be held on 28th September.

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

November 1955

A Meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on Friday, 18th November, 1955. The President, Mr. H. J. Malkin, was in the Chair.

Mr. S. Bender read a short paper on

Ovarian Function in the Absence of the Uterus

(This article appears on page 204 of this issue)

Discussion

Mr. N. L. Edwards asked if the small knobs of tissue at each end of the transverse fold of peritoneum had been examined for endometrium.

Mr. S. B. Herd had seen 2 similar cases. He had also reluctantly performed a hysterectomy on a girl of 8 for supposed malignancy. Now, at the age of 25, she had returned to see him. She was married and had adopted 2 children. Her general appearance and breast development were normal. The external genitalia and vagina were fully developed, and one ovary felt cystic.

Mr. C. H. Walsh thought the cyst in the right ovary might be a haemorrhagic corpus luteum, and there was no need to postulate endometrium in it. He had found cystic follicles in ovaries conserved at hysterectomy, but had never seen malignant change.

The President had recently had a patient who died of ovarian carcinoma from the ovary he had conserved at hysterectomy some years before.

Mr. Bender in his reply said he had mentioned endometriosis to make it more interesting. At a British Medical Association Meeting Professor Strachan had been in favour of removing the ovaries at the time of hysterectomy, as he had seen malignancy occur.

Dr. R. E. Rewell read a paper on

What is the Normal Cervix?

The following investigation was started some four years ago with two objects. (*a*) To determine the incidence of minor histological abnormalities in cervices removed surgically not for primary disease of the structure. (*b*) To devise a practicable method of histological examination that would find as many as possible of the unsuspected early cancers known to occur there. Both these aims, if achieved, would help the surgeon to know if a given cervix could be regarded as "normal" and that further treatment of the patient was unnecessary.

Materials and Methods Employed. The ideal way to ensure that all features of a given cervix were examined, would be to cut serial sections of it. This term has frequently been employed to cover "multiple sections", but if used in its proper sense would mean the preparation and examination of hundreds, if not thousands, of sections from each specimen, obviously an impracticable procedure. The services of different surgeons were thought to offer as good a method as any of choosing unselected series and so those coming from one were cut four times radially, from others twice sagittally and those coming as part of hysterectomy specimens only once at random. A few were cut differently in error. The figures are shown in Table I. The abnormalities noted in each case were: (1) presence of infection, (2) of infection with ulceration in one or more sections, (3) epidermidization, (4) the presence of follicles and (5) the presence of a polyp. The number of examples of each condition are shown in Table II while Table III shows the correlation of the different conditions. No significant differences were found whether one, two or four sections were cut, except, of course, for the presence or absence of polyps.

Table I
Numbers of Routine Sections of Cervix

One only	292
Two sagittal	213
Three radial	17
Four radial	93
Five radial	1
Total	616

Table II
Occurrence of Abnormalities

Infection	300
Infective ulceration	39
Epidermidization	79
Follicles	70
Polyp	41

Table III
Correlation of Data

Polyp and infection	25	41 polyps
Polyp and ulceration	3	
Follicles and infection	37	70 follicles
Follicles and ulceration	0	
Epidermidization and infection	69	79 cases of epidermidization
Epidermidization and follicles	7	

Results. Table III shows that whereas nearly three-quarters of the polyps were associated with infection,

only half of the follicles were. Most of the cases of epidermidization, however, showed obvious infection. These correlations are well known, of course, but Dr. Rewell had not seen detailed figures to support them.

Excluded from the Tables is all mention of malignancy. None of the cervices included in the series showed this change grossly and in only 2 was unsuspected malignancy found microscopically. In one, intra-epidermoid cancer was widespread over the surface of the whole cervix and vagina and would obviously have been seen in any random section. In the second case a small area was found in one of two sagittal sections and not again, despite repeated resectioning. It is interesting to note that this patient was dead within 6 months of rapid local recurrence.

The figures, therefore, give no guide to the number of sections that must be cut if early malignancy is to be excluded, as the number of early cancers found is so small.

Addendum on the Use of Smear Techniques. The above paper was prepared a year ago and not given owing to lack of time at the meeting for which it was made ready. Since then Dr. Rewell had gained experience of the Ayre's smear technique. Of the last 200 smears 5 were thought to show malignancy and 3 of these have been confirmed by ring biopsy. One awaits biopsy and in the other case the surgeon has deferred biopsy and intends to take another smear after an interval.

These smears were taken from women over an agreed minimum age attending the clinics of the different surgeons at the Women's Hospital, Liverpool, the minimum being set in each case by the surgeon concerned. In none was malignancy suspected. During the same time 306 cervices have been removed operatively for non-malignant conditions and only 1 unsuspected malignancy found. The superior usefulness of the smear technique is held to be obvious. These figures have been included in a letter published recently (Rewell, 1955).

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Discussion

Mr. N. L. Edwards had had the opportunity of working with a pathologist who undertakes the Papanicolaou stain, and routine smears are taken from patients of all ages who attend the clinic. There had been 3 patients in their twenties with carcinoma of the cervix. A biopsy from an apparently normal cervix was a bit hit and miss, whereas a positive smear might be obtained in both invasive and intra-epithelial carcinoma. Mr. Edwards preferred the Papanicolaou method, a spatula must easily slip over areas in an irregular cervix, whereas it is simple to pick up material from the posterior fornix.

Dr. R. E. Rewell in his reply said that Dr. Osborne of Derby had shown that any competent pathologist can do a Papanicolaou smear especially from the cervix or ascitic fluid; he found the method, however, time consuming and he used the Ayre technique.

Mr. H. V. Corbett read a paper entitled

Why Prolong Labour?

(This article appears on page 201 of this issue)

Discussion

Mr. C. J. K. Hamilton was glad to come back to the term uterine inertia. He had seen hypo- and hypertonic actions treated in various ways when the trouble was a 10 pound baby. He was not so liberal in his use of pethidine.

Mr. P. Malpas mentioned a series of post-mortems on patients who died after long labours. Severe pressure and gangrene of the lower uterine segment were evident. The difficult time is late in the first stage when progress hangs fire. The state of the caput and pressure on it should be the deciding factors on when to interfere.

Mr. S. Bender: The observation of these cases is with the registrar. The sun should not set twice on the same labour, and though the results could be excellent with the patient in labour 48 hours, psychic troubles were rarely mentioned. Most people have a high Caesarean section rate and Mr. Bender thought Mr. Corbett was fighting unnecessary foes. The academically minded obstetrician made as ready a resort to Caesarean section as the rest. He preferred the term inefficiency to inertia.

Mr. N. L. Edwards asked the Society what were the values of the various signs of foetal distress. He thought perhaps a little bit too much importance was placed on slight variation in foetal heart rate.

Mr. J. G. Wigley said that early intervention once occurred because of the risk of puerperal fever. Maternal mortality was now small and so search must be made for ways of reducing the foetal loss. At one time meddlesome interference was not allowed and patients were left too long in labour, but now it was the baby who should have the attention.

Mr. S. B. Herd thought that the difference in the ineffective and the inco-ordinate uterus was the way the mother and the baby could stand up to interference. In the latter condition both were "shock prone", but in the former case the patient might be tired from lack of sleep, but stood up to trauma and blood loss more easily.

Mr. H. Roberts mentioned the difficulty in determining the time of onset of labour. He asked Mr. Corbett to what the term inertia referred: the contractions, the effect on the cervix, or the time of labour. If the last, prolonged labour is the better term.

Mr. Corbett replied.

Mr. P. Malpas read a paper on

A Criticism of the Hypothesis of Placental Insufficiency

(This article appears on page 199 of this issue)

Discussion

Mr. C. H. Walsh referred to the discarded placental theory for the cause of toxaemia of pregnancy, and that labour occurred late in many cases of anencephalus. He asked for an explanation of premature delivery according to this theory.

Mr. S. Bender said that the placenta had two main functions—it was an organ of transfer, and it produced hormones. Why had this large production of hormones little effect on the foetus?

Mr. H. Roberts asked if the acetylcholine extracted from the placenta bore any relation to the foetal adrenal.

In his reply Mr. Malpas agreed that prematurity might be a loophole in his theory.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

December 1955

A Meeting of the North of England Obstetrical and Gynaecological Society was held at Sheffield on 16th December, 1955. The President, Mr. H. J. Malkin, was in the Chair.

Mr. J. B. Cochrane and Mr. R. B. Zachary reported the case of

An Unusual Perineal Tumour at Birth

In these days of changing trends, it is not unusual to find the infant born with an interesting deviation from the normal immediately to be spirited away with all speed from the obstetrician and placed in the lap of his paediatric colleague. This case record illustrates one such infant, who, in fishing parlance, did not get away, at least, not until the time was opportune.

Mr. Cochrane first encountered the infant when he was still *in utero*, for in February, 1955 his mother was referred to Mr. Cochrane at the 33rd week of her gestation on account of hydramnios. Hydramnios was present. An X-ray examination showed no skeletal deformity of the foetus, and the pregnancy continued until 20th March, 1955, when a male child was born at home after a normal labour. When the doctor examined the child he judged him to have a spina bifida and large meningocele and Mr. Cochrane was called in consultation.

Examination showed a large, cystic swelling distending the whole pelvic floor and bulging through it between the anus and sacro-coccygeal region. There was no evidence of any connexion with the spinal meninges nor of spina bifida, and the baby's head was normal without suggestion of hydrocephalus. Mr. Cochrane presumed that a developmental retroperitoneal cyst was present and arranged for hospital admission. Further clinical examination showed the cyst to be translucent and to extend above the limit of the finger on rectal examination. It swelled and tensed when the infant cried, but there was no propagation of a thrill to the anterior fontanelle, and no other abnormality present. As a plain X-ray showed a normal spine it was deemed safe to withdraw 5 ml. of the fluid by aspiration, replacing with the same amount of air. The resultant X-ray demonstrated a large retro-peritoneal cyst, which, according to the radiologist, extended up to the diaphragm and the upper limit of which was detailed by the air bubble. The results of the biochemical examination of the cyst fluid were inconclusive.

An attempt to outline the extent of the cyst by injecting Viskisol 6 showed a retro-peritoneal extension which communicated through a narrow neck with a big perineal cyst. From these investigations it was thought that the condition was operable, but that as the technical procedure might be difficult the child was referred to the care of Mr. Zachary at the Children's Hospital, Sheffield.

Mr. R. B. Zachary stated that the differential diagnosis consisted of (*a*) an anterior meningocele, (*b*) duplication of the rectum and (*c*) teratomatous cyst.

Operation was decided, and dissection of the cyst proved easy along the posterior border of the tumour, but a short way up the anterior surface yielded a small area densely adherent to the posterior rectal wall. Doubt arose whether this was duplication of the rectum, and a frozen section was made to determine the nature of the lining epithelium. However, a few hairs were found within the cyst cavity, endorsing the initial diagnosis of teratomatous cyst, and with further dissection the cyst was removed *in toto*. The recovery of the infant was uneventful, and a reasonably sound scar with good anal sphincteric control obtained.

Discussion

Dr. N. Lissimore asked from which tissue the tumour arose.

Mr. T. B. Fitzgerald thought that if this child had been a girl the operation might come within the province of the gynaecologist.

Professor Jeffcoate questioned the meaning of "the perineum". If the area behind the anus is the perineum, then it would be right for the gynaecologist to operate there.

Mr. Zachary in his reply said that many of these tumours are solid and these present difficulty in removal. He deferred his decision on the political question.

The President, Mr. H. J. Malkin, delivered his address on

Some Early Obstetricians and Their Contribution to Midwifery

It seems reasonable to claim that since reproduction is one of the essentials for continued existence, the art of Obstetrics is the oldest of the three main branches of Medicine. Though Man has been in existence for so long a time, history is very incomplete, and we do not know much of the difficulties of our more primitive forebears. From Ariege, in France, we have the first evidence of the Physician about 20,000 B.C. Lack of knowledge and skill has been compensated for in the drawing by an impressive appearance. This practice of wearing abnormal, or, at least, unusual garb, still obtains to this day in some areas as is shown by the dress of a 20th century Medicine Man. Even in civilized communities a certain type of dress is regarded as essential for the budding consultant.

Before naming some of the personalities of our

specialty and their achievements, Mr Malkin drew attention to that most disconcerting gap in history—the Dark Ages—when the centuries rolled by with little progress in Medicine. Christianity was in many ways an obstruction, as the belief held by ardent Christians that cleanliness was unholy did much to cause unnecessary suffering. In Eastern Mediterranean countries there were some advances, and at the times of the Crusades the standard of medical skill on the side of the crusaders was considerably lower than that of the Saracens. It was the custom of both sides to lend assistance between battles, and it is recorded that a Saracen doctor was dismayed at the treatment a Frankish doctor gave his own sick. Apart from a small amount of knowledge acquired during the Crusades, we see virtually no light until the Renaissance.

The first physician of whom we have much knowledge is Asklepios, or, as the Romans called him, Aesculapius. There is some confusion about his origin. According to some he is the deified Imhotep who built the first pyramid about 3000 B.C. Aesculapius of mythology is reputed to be the son of the god Apollo and Coronis, a mortal woman, and is said to have been born by Caesarean section. His healing power was such that Hell was rapidly becoming depopulated, and Pluto urged Zeus to do something. The latter obliged by hurling a thunder bolt at the offender. Aesculapius's daughter was Hygeia.

The cult of Aesculapius soon resulted in temples on Cos, Triccae and Epidaurus, and later the Asklepians specialized in Medicine, their temples being the forerunners of a medical school, and containing wards for the sick. Two points of interest are that anyone likely to die was turned out into the countryside, and no maternity cases were at first admitted.

Cases of sterility did go for advice, and in the Museum at Epidaurus there is the record of a lady named Cleo who did conceive but the pregnancy continued for 5 years. Further enquiry showed that her request had made no mention of delivery. Later she was delivered of a little boy just over 4 years old. The theatre at Epidaurus is still used each year, and the acoustics are unbelievably perfect.

In this Asklepian period the outstanding figure was Hippocrates, born in Cos in 460 B.C. He was a profound investigator and observer and a great teacher, and his main contribution was that it was the function of the physician to assist the natural forces in their reaction to disease. Hippocrates realized, too, that in certain cases of contracted pelvis delivery could be effected by internal version.

The first obstetrical specialist was Soranus, born at Ephesus in A.D. 98, some 30 years after Paul wrote his Epistle to the Ephesians. His book *De Mortis Mulierum* was the work on which 1,400 years later the *Byrthe of Mankynde*, translated from the German textbook *Rosengarten* by Rosslin, was based. Soranus advocated overcoming pelvic contraction by version, and he taught that delay in labour might be due to an undilating cervix which "the midwife should stretch with the fingers".

It was Soranus who gave the first accurate description of puerperal fever, the cause of which might be from "abortions or labours improperly attended", and he also held advanced views on the care of the newborn. He poured scorn on many accepted treatments of prolapse, such as "suspending the patient head downwards on a ladder for a day and a night", and professed gentler methods.

Galen was born half a century later than Soranus. He was a successful physician and a prolific writer, and his observation and methods influenced medicine for the next 1,400 years. That many of his dicta were false is reasonable. Anatomy was little understood, and was studied mainly in animals, though in the reign of Alexander the Great dissection of criminals, alive or dead, was permitted. Galen's main contribution to obstetrics was his teaching that the foetus performed no active movement to assist delivery, but was the passenger only. During the Dark Ages progress was at a standstill, and the main problems to be solved were then, as now, those of delayed labour, toxaemias, haemorrhages and infection. The commonest method of treating delayed labour was to shake the baby out, but version, as suggested by Hippocrates, was not revived until Paré, in the 16th century, became interested in the manœuvre. Up to then the main treatment was to lift and drop the patient, as it was thought that the pelvis separated to let the child out and all that was necessary was a few good bumps. Little is recorded of the treatment of haemorrhage and infection, and it is doubtful whether toxaemia other than fits was recognized.

The next landmark was the first successful Caesarean section in 1500, performed by a peasant on his wife. There were 15 successful Caesarean sections in the 16th century, and this was not equalled until the 19th century. It was not until suturing of the uterus became the accepted method that the mortality figures dropped.

Ambroise Paré was born in 1510 and became an army surgeon. During the treatment of a number of wounded he omitted to cauterize the wounds of one patient. Realizing his mistake during the night, he rose early and was amazed to find the man a great deal fitter than those whose wounds had been cauterized. He became surgeon to successive kings of France, and was one of the few to survive the Massacre of St. Bartholomew. Paré introduced the ligature to control bleeding, and revived version as a method of overcoming minor degrees of contracted pelvis, a method that was used to save the life of his own daughter.

Paré, though a Huguenot, stayed in his native land. His compatriot, William Chamberlen, another Huguenot, having witnessed the battle of Jaruac, fled with his wife and family to England. Chamberlen had 5 children; the oldest and youngest, both named Peter, were interested in obstetrics. Peter the Elder was Physician to James I and his Queen, Anne of Denmark. Both brothers fell out with the College of Physicians, partly because they pushed the suggestion of a "Society of Midwives". Peter the Elder was probably the inventor of the obstetric forceps, and the secret was kept in the Chamberlen family for three generations. Hugh

Chamberlen's claims for them were greatly exaggerated.

François Mauriceau was born in 1637 and became one of the leading obstetricians in the world. His book *Observations on Pregnancy and Accouchement*, translated into English by Hugh Chamberlen, earned Chamberlen a small fortune. Mauriceau's contributions to obstetrics were his book and his skill in breech delivery.

In 1651, William Harvey published the first original book on Midwifery in English, and in the chapter "De Partu" recommended patience, watchfulness and gentleness.

William Smellie was born in Lanark in 1697 and went into practice there. Later he went to Paris and London where he developed a large obstetric practice. Smellie can claim to be the first to instruct by the use of a mannikin. He had a detailed and accurate knowledge both of the physiology and pathology of labour. During his teaching years he trained 900 students, and gave 280 courses of lectures, charging 3 guineas a course, or 20 guineas for a year's tuition. The students had to pay six shillings for the support of the "poor labouring women". We owe to him not only the detailed method of teaching by the mannikin, but a proper understanding of the mechanics of labour, an appreciation of pelvic measurements and a realization of the difficulties which followed if the measurements were smaller than required for a particular child.

Early in the 18th century, the brothers William and John Hunter were born in East Kilbride, and their main contribution was anatomical. To them we owe our knowledge of foetal and placental circulation, the retroverted gravid uterus and the description of the decidua. William Hunter, in contrast to Smellie, was an advocate of masterly inactivity, and his conservatism which extended to conditions such as unfavourable face presentations and retained placenta influenced British Obstetrics adversely for many years. There is little doubt that this exaggerated belief in non-interference was the cause of death, amongst many others, of Princess Charlotte, heiress to the throne, and wife of Prince Leopold of Saxe-Coburg in 1817.

In 1745, in Dublin, Bartholomew Mosse opened a House for Poor Lying-in Women. Later a new hospital was built, but before the Rotunda was completed, Mosse, the first Master, had died. He was succeeded by Fielding Ould who recognized that the foetal head was elliptical, and that if the long axis of the ellipse were in the same plane as the birth canal, that is in incomplete flexion, there was likely to be difficulty.

And now a reference to Puerperal Fever, and particularly the work of Charles White, Alexander Gordon, Oliver Wendell Holmes and Ignaz Semmelweiss. This condition, though prevalent in hospital practice, was not recognized as a disease. When we consider the overcrowded conditions in maternity hospitals in the 18th century, the results are not surprising. In 1790 Charles White was appointed to the Lying-in-Charity in Manchester. He wrote a treatise in which he advocated what is now known as Fowler's position, fresh air, cleanliness of the patient, and, for the attendants, cleanliness of hands and clothing—startling suggestions in those days.

In 1795 Alexander Gordon of Aberdeen demonstrated how infection occurred in patients attended by a midwife who had previously attended an infected case. Oliver Wendell Holmes's outstanding contribution was his insistence that puerperal fever was a contagious disease.

About the same time, Ignaz Semmelweiss was struck by the high death-rate occurring in the wards attended by students compared with those attended by midwives. The death of his pathologist friend, Kolletschka, from septicaemia following a prick while doing a post-mortem on a puerperal fever case, brought home the probable state of affairs. He instructed his students to wash their hands in a solution of chloride of lime, and the mortality fell. Semmelweiss was unpopular for his unorthodox views; he lost his post, and later his reason gave way.

The results of the practice of these four men were not bettered to any great extent till the advent of the sulphur drugs in 1936.

In the last 200 years there have occurred most of the outstanding advances in obstetrics—advances that we now take for granted. First the establishment of Maternity Hospitals, then the descriptions by Rigby of accidental and unavoidable haemorrhage, thirdly the treatment of contracted pelvis by induction of premature labour, and later pelvic measurements. In the 19th century notable contributions were the auscultation of the foetal heart by Lejumeau, and the modification of the Chamberlen forceps by Tarnier. Version, originally practised by Hippocrates and Soranus and re-introduced by Paré, was advocated by Braxton Hicks as a method of coping with intermediate degrees of pelvic contraction or controlling the bleeding from placenta praevia.

About this time Credé became Physician-in-Chief at the Charité in Berlin, where he taught a method of expulsion of the placenta by massaging the fundus, and a later modification in which he recommended forceful compression shortly after delivery of the foetus. To Credé belongs the credit of controlling ophthalmia neonatorum by the instillation of silver nitrate.

In 1848 John Lever of Guy's Hospital described a case of puerperal convulsions, drawing attention to the fact that she had oedema and albuminuria. Brief reference must also be made to blood transfusion, first tried in 1667 with blood from a lamb, but in 1824 James Blundell first used human blood with success. It has been impossible to mention X-rays or the revolutionary work of Ballantyne in antenatal care. Reference has been made to a few of the personalities and landmarks that deserve attention, but many important people remain unmentioned and the story is incomplete.

Mr. Malkin was thanked for his address and for his care of the Society during his year as President by Mr. J. W. Hunter (Manchester), Mr. C. H. Walsh (Liverpool), Professor A. M. Claye (Leeds), Mr. F. Stabler (Newcastle) and Mr. L. B. Patrick (Sheffield).

BOOK REVIEWS

"Perinatal Mortality in New York City." Analyzed and reported by S. G. KOHL, M.S., M.D., Dr.P.H. Pp. xxi+112, with 67 tables. Harvard University Press, 1955. London, Cumberlege. Price 20*s*.

THE New York Academy of Medicine sponsored this analysis of 955 of the stillbirths and neonatal deaths in that city in 1950–51. It is a meticulous review which offers much food for thought to obstetricians, paediatricians and public health authorities in all countries, including those where conditions are not parallel to those in New York, where, for example, a home confinement is exceptional.

The value of this report is threefold. Firstly there are the clinical observations made. Foremost among these is the conclusion that 35 per cent of all the deaths, and a higher proportion of those in mature babies, were preventable. Errors in medical judgment and techniques and inadequate antenatal care were the outstanding responsible factors. But there are many other challenging conclusions: that it is among the mature babies that the attendants have the greatest opportunity of saving lives; that birth trauma is still a major factor, for it caused 11 per cent of the stillbirths and over 20 per cent of the early neonatal deaths; that 40 per cent of the deaths in babies delivered abdominally were preventable; that the stillbirths associated with maternal toxaemia carried a preventability rate several times that observed in the absence of toxaemia.

Secondly, this review provides yet another evaluation of the accuracy, or rather inaccuracy, of the information received and the statistics compiled by local and national authorities. Disagreements between clinical records, pathological findings and death certifications were common, with the last most often inaccurate. Hardly less valuable is the detailing of the methods of sampling, analysis and weighting employed in this report. A refreshing feature of Dr. Kohl's work is that he admits the shortcomings of his review, notably that for better interpretation a study of surviving babies should have been included. However, constructive suggestions are offered for future investigations into this or similar problems.

Certain difficulties are inherent in analyses such as this, in particular that the same case cannot be used as both test and control. Nevertheless this terse report on the perinatal mortality in one city in one year is so illuminating that it might justifiably be subtitled *multum in parvo*.

"Analgesia for Midwives." By HILDA ROBERTS, M.R.C.S., F.F.A.R.C.S., D.A., D.C.H. Hon. Research Assistant, Institute of Obstetrics and Gynaecology, Hammersmith Hospital, London. Pp. 68, with 25 figs. and 5 colour plates. E. & S. Livingstone, Edinburgh and London, 1955. Price 10*s*. 6*d*.

THIS small book is based on the author's lectures to midwives. The first five chapters cover the main subject matter. The presentation is pleasantly informal, but mention might have been made of the antidotal value of N-allylnormorphine and of the qualities of lignocaine. The midwife might also be interested to know why there is a hole in the metal handpiece of some but not all gas-and-air machines. The last three chapters are valuable additions on the care of the unconscious patient, the resuscitation of the newborn, and the preparation of apparatus and instruments for regional analgesia.

The book is beautifully produced, but even in these days of inflation 126 pence seems an excessive price for 65 pages of text. Perhaps the price could be reduced by sacrificing the colour plates which are attractive to the eye but add little to clarity.

"The Year Book of Obstetrics and Gynecology." Edited by J. P. GREENHILL, B.S., M.D., F.A.C.S. Pp. 544, with 83 figs. The Year Book Publishers, Incorp., Chicago and Interscience Publishers, Ltd., London, 1955. Price 45*s*.

THIS volume contains a critical analysis of articles abstracted from journals received between July, 1954 and July, 1955 and it maintains the high standard of its predecessors. At the same time it is to be recognized that it is devoted in preponderant measure to American literature. This becomes apparent when the articles abstracted are numerically related to their source of origin. Thus approximately 200 of the articles appeared in American obstetrical and gynaecological journals and, in addition, many came from American journals of a general nature, whilst other countries are represented approximately as follows: Great Britain and the British Commonwealth, 35 articles; Scandinavia, 12; Switzerland, 10; France, 9; Germany, Belgium, Spain and Argentine, 1 each. These figures demonstrate that the aim of the book is much more restricted than, for example, the Review of Current Literature in *The Journal of Obstetrics and Gynaecology of the British Empire*.

The Editorial notes in small type richly scattered throughout the volume constitute one of the most valued features and, in the sense that they are more Catholic in their survey, help in some measure to offset the parochial outlook of the book. It is only right to state that the Year Book does not claim to cover world literature. It is essentially a compact, valuable and critical analysis of American work.

"Modern Trends in Blood Diseases." Edited by JOHN F. WILKINSON, M.D., M.Sc., F.R.C.P., F.R.I.C. Pp. 359. Butterworth, London, 1955. Price 65*s*.

THIS recent addition to the "Modern Trends" series is primarily for the haematologist and physician, but

includes sections of interest to the obstetrician and gynaecologist. These are the chapters on isoimmunization to blood group antigens and on anticoagulant therapy, and the portion of the account of paediatric haematology which relates the normal variations in blood values in the newborn and discusses the blood dyscrasias of neonatal life. In addition, reference is made to the relationship between Vitamin B_{12} and megaloblastic anaemia in pregnancy and puerperium, and to the presence of hypercupraemia in normal pregnancy.

"The Pregnancy Toxaemias or the Encymonic Atelositeses." By G. W. THEOBALD, M.A., M.D., F.R.C.S., F.I.C.S., F.R.C.O.G., M.R.C.S. Pp. xiv+488, with 56 illustrations. Henry Kimpton, London, 1955. Price 63*s*.

THIS is the fifth book in the English language on the subject of the toxaemias of pregnancy which has appeared during recent years, so that the Anglo-American world of Obstetrics need have no fear that it is not being kept up to date on the progress being made in this difficult field. The Ciba Foundation's publication (1950) dealt with the papers presented at a symposium on the subject: a most useful meeting which we hope will soon be repeated. Dr. Dieckmann's noble volume (1952) is a magnificent source book for all those interested in any branch of the subject; Dr. Sophian's interesting book (1953) was largely devoted to the author's ideas on the utero-renal reflex; Dr. Page's brilliant essay (1953) has been a boon to all those who required a balanced résumé of modern work and thought on the toxaemias. Dr. Theobald's five-hundred-page long book, almost encyclopaedic, consists of an outstanding critical review of the whole subject. He writes with the greatest authority for not only has he made many lasting contributions to our knowledge of disordered physiology in pre-eclampsia but his wide clinical experience in different climes has enabled him to survey the whole horizon instead of the restricted view obtained by those of us whose experience is obtained in one community or who have devoted our interests to one particular part of the problem.

The late Professor Newton introduced the term *The Maternal Syndrome* to describe the whole sequence of physiological changes consequent on the establishment of pregnancy. Dr. Theobald has modified the term to *The Pregnancy-Lactation Syndrome* and Part I of his book deals with the physiology of pregnancy. Here will be found a splendid review of our knowledge on all the changes in metabolism occurring in pregnancy. The reviewer would particularly draw attention to the chapters on water metabolism and water diuresis in pregnancy. It is in this field that the author has made many fundamental contributions. It is quite extraordinary how some of Theobald's work on the effect of posture on diuresis is being re-discovered twenty years after his original publications! Progress in the field of the physiology of pregnancy is for ever active and it is very difficult and almost impossible to be completely up to date in a large book of this sort.

Part II consists of a description of toxaemia of pregnancy in all its various forms and with some logic Dr. Theobald includes as a "toxaemia" any deviation from the normal pregnancy-lactation syndrome. This section makes excellent reading and is a well documented account of the major forms of toxaemia including the clinical features and pathological findings.

Part III deals with the various hypotheses advanced to explain the major forms of toxaemia. Dr. Theobald gives a formidable list of sixteen criteria which must be fulfilled if any hypothesis is to have a prospect of being acceptable. The placental hypothesis is regretfully but firmly discarded. The young obstetrician of today who so facilely accepts the teaching that under certain conditions there may be increased intra-abdominal pressure leading to placental ischaemia might well ponder on the work done by Theobald and Verney many years ago showing that there was in fact no rise in intra-abdominal pressure during pregnancy even in the primigravida. Further, he points out that in fact the incidence of eclampsia and pre-eclampsia is very low in hydramnios occurring in single pregnancies. The author rejects convincingly the renal-ischaemic hypothesis of Sophian. Perhaps we may anticipate a notable academic clash? The author then develops his well-known nutritional-mechanical hypothesis and reference to the book must be made for a description of this, for it is impossible to do justice to the hypothesis in a few sentences.

Part IV deals with the treatment of pre-eclampsia and eclampsia. Table 27 is quite fascinating for it sets forth all the methods of treatment which obstetricians have in their desperation used in handling the eclamptic patient.

It is not the reviewer's task to take issue with an author over minor matters and there are, of course, many points on which the reader is bound to disagree but these are relatively unimportant. The use of the expression *the encymonic atelositeses* as a synonym for the toxaemia of pregnancy is surely an affectation and, for the increasing number of obstetricians whose classical studies included a smattering of Latin but no Greek, the words are tongue-twisting and meaningless. Dr. Theobald has, however, obviously enjoyed retaining this phrase in spite of the reactions that he must surely have expected!

The book does great credit to Dr. Theobald and to our specialty as a whole. Recently one of our leading physicians, Professor Pickering, in his book on High Blood Pressure, has jibed at the obstetrical world for retaining the expression *toxaemia of pregnancy* as a term including such strangely different diseases as hyperemesis and pre-eclampsia. He feels that it reflects an inability to throw off the chains of the past or as indicating an utter confusion of mind. Perhaps a perusal of Dr. Theobald's book would show, in fact, how these may be regarded as deviations from the normal pregnancy-lactation syndrome about which he writes so clearly and logically. The book must be read by all obstetricians interested in the toxaemias of pregnancy.

Robert Kellar

"The Boke of Chyldren." By THOMAS PHAIRE. Pp. 76. E. & S. Livingstone Ltd., Edinburgh and London, 1955. Price 7*s*. 6*d*.

The Boke of Chyldren is the first English textbook on

Paediatrics, written by Dr. Thomas Phaire and published in 1545. It has now been reprinted in its entirety with the 16th century spelling retained but happily in 20th century print. With occasional reference to a most useful glossary the book is easy to read.

That Thomas Phaire must have been an excellent physician is shown by the many astute and thoughtful clinical observations in his book. Here are two examples. The first is of particular interest because of the attention now being paid to the dangers of over-heating the cold premature infant: ". . . whan a mẽber is vtterly benummed and taken through colde, so that the pacient can not feele his lymmes, nor moue them according to nature, by reason of the vehemẽt of cõgelaciõ of y^e^ bloud, in such case y^e^ chiefest help or remedy is not to set thẽ to the fyer to receyue heate, for by that meanes, lightly we se that euery one swowneth and many dye outryght, but to sette the feete, legges and armes, in a payle of clere colde water, which immediately shall dissolue the congelacion, . . ." The second example shows that he clearly recognized the commonest cause of cough in children to be in upper respiratory infections: "The cough in childrẽ for the moste part, procedeth either of a cold, or by reason of reumes, descending from the head into the pipes of the longes or the breast, . . ."

More than half the text is devoted to treatment which is perhaps of less interest, although compared with many writers of the same period his prescriptions are relatively simple and "holsom" and who knows what therapeutic treasures may lay hidden in them! The reviewer was glad to note that when dung was prescribed in any form it was usually "seethed" before application. Dr. Phaire sensibly knew when to withhold medicines:

"*Of Smal Pockes and Measilles*

Remedye: The best and moste sure helpe in this case, is not to meddle with anye kynde of medicines, but to let nature worke her operaciõ . . ."

Altogether thirty-nine disorders of health in childhood are discussed. A similar list of the commonest diseases today would not be very different.

This is a delightful book which should give pleasure to all members of the medical profession. We should be grateful to Professor Neale and Dr. Wallace for making it available and for their interesting introduction and annotations.

J. P. M. Tizard

REVIEW OF CURRENT LITERATURE

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PREGNANCY

87. Treatment of Hyperemesis Gravidarum with ACTH.
By P. A. JARVINEN and V. J. UUSPAA. *Ann. chir. gynaec. fenn.*, **44**, 170–176. 1955. 17 refs.

Twenty patients with severe hyperemesis were investigated in hospital. The urinary corticosteroids were found to be low and the patients were treated with daily doses of Cibacthen gel injected intramuscularly to a total of 100–120 units. All recovered permanently within ten days except two who relapsed and were finally cured by further injections of 20 units for five days. The corticosteroids in the urine increased during treatment.

The author believes that there is hypopituitarism present in hyperemesis due to a temporary change in production of steroids inhibiting release of ACTH.

[No comment is made on the possible psychological effect on the patient of hospitalization and daily injections.]

D. M. Sheppard

88. Retroperitoneal Haemorrhage in Pregnancy.
By H. C. CALLAGHER. *Med. J. Aust.*, **2**, 291–292. Aug. 20, 1955. 4 refs.

Placental separation, acute hydramnios, toxaemia and retroperitoneal haemorrhage occurred coincidentally in the one patient. When 26 weeks pregnant she was seized with acute pain in the left loin when hanging out the washing. On admission to hospital some hours later it was found that there was hypertension, albuminuria, shock, together with a tense tender uterus the size of a 36-weeks pregnancy, and no signs of foetal life.

The membranes were artificially ruptured, an intravenous drip administration of pitocin was instituted and a blood transfusion given. There was no external blood loss. A diagnosis of retroperitoneal haemorrhage was made, and in view of the acute uterine distension it was decided that there was rupture of the left ovarian vein. The abdomen was opened, and hysterotomy performed when partial separation of the placenta was found. Retroperitoneal haemorrhage was found at the outer end of the left broad ligament extending up to the renal pouch and the left renal vein was found torn five centimetres below its junction. Haemorrhage was controlled and the patient recovered.

The author reviews the literature, citing Zummo *et al.* (*Surg. Gynec. Obstet.*, 1952, **95**, 51) who added four

cases to the 44 already recorded. Of these 44 only 7 survived. Usually the haemorrhage was associated with aneurysm of the splenic or renal arteries.

Callagher wonders whether there was an association between the primary retroperitoneal haemorrhage and the hydramnios and toxaemia, whether the placenta separated as a result of the acute hydramnios or of the pitocin drip, and whether the toxaemic manifestations were due to the disturbance of the blood supply to the left kidney.

S. Devenish Meares

89. **Rupture of Splenic Artery Aneurysm in Pregnancy.** By L. O. S. POIDEVIN. *Med. J. Aust.*, **1**, 922–923. June 18, 1955. 7 refs.

The patient aged 24 years was admitted to the Queen Victoria Maternity Hospital, Adelaide, when 36-weeks pregnant in her sixth pregnancy. During the preceding 10 days she had experienced 3 nocturnal attacks of sudden sharp epigastric pain which woke her and caused her to sit up and gasp for breath. The attacks were of such short duration that medical aid was not sought. On the day of admission she had been in good health but in the evening was seized with severe pains in the epigastrium with dyspnoea and collapse. She presented the picture of a severe diffuse intraperitoneal haemorrhage.

She was resuscitated by transfusions and laparotomy was done 6 hours after admission. Many pints of blood escaped. After emptying the uterus it was found that the lesser sac was filled with blood clot and fresh blood came freely from the foramen of Winslow and the gastric wall was indurated with haemorrhage. The patient's condition did not justify further surgical procedure and she died while the abdomen was being closed. At autopsy a ruptured aneurysm was found on the middle section of the splenic artery.

Probably less than 30 cases of this condition have been reported of whom only two have survived.

S. Devenish Meares

90. **Antenatal Pulmonary Embolism.** By E. M. SIBTHORPE. *Brit. med. J.*, **2**, 1063–1064. Oct. 29, 1955. 2 refs.

Three cases of antenatal pulmonary embolism are reported and bring the total number of cases recorded since 1922 to 28.

The first concerned a 7-gravida aged 38 years, at the 38th week of pregnancy; the second a 27-year-old primigravida who was 36 weeks pregnant, and the third a 2-gravida aged 23 at the 28th week of pregnancy. One of the patients, the primigravida, died, and only one of the infants was born alive.

Ullery's review of 25 cases of embolism revealed an incidence of 18·5 per cent, with a mortality rate of 60 per cent, in a total of 135 cases of antenatal thrombosis. Pulmonary embolism occurred in the same number of cases of thrombosis, whether on anticoagulant therapy or not, but no fatalities occurred in patients who were given anticoagulants.

The present author quotes Sachs and Labate (*Amer. J. Obstet. Gynec.*, 1949, **57**, 965) to the effect that anticoagulants themselves are not without risk and goes on to indicate that they are not yet of proved value. For these reasons her three cases were not treated with anticoagulants.

Ligation of the inferior vena cava was not employed in view of the poor end-results and the danger of further embolism while emptying the uterus in order to give access to the vessel. Her cases were treated symptomatically. Elevation of the foot of the bed and free movement of the patient's legs were considered to be valuable conservative measures and noradrenaline was found to be very effective in the treatment of the associated shock.

R. W. Grayburn

91. **Thrombophlebitis in the Pregnant Woman.** (Les thrombo-phlébites de la grossesse.) By P. MORIN and J. CHABRIER. *Gynéc. Obstét.*, **54**, 400–417. 1955. 9 figs.

The clinical features of thrombophlebitis occurring in the course of pregnancy do not differ from those of post-partum thrombophlebitis. Diagnosis does not present difficulties. The onset, however, is less dramatic and the clinical picture may take several days to establish itself. The writers failed to establish any relationship between the stage of pregnancy and the appearance of the thrombosis. Cases of thrombophlebitis in pregnancy appear to predispose more to vascular troubles than to trophic disturbances. The remote prognosis is satisfactory although immediate function may be poor.

Having shown that there is no blood dyscrasia and that the plasma proteins are normal these cases should be treated by anticoagulants. The writers' preference is for the use of Heparin, which causes no danger to the child. The rest of the treatment is symptomatic.

D. Maxwell

92. **Urological Complications in Pregnancy.** By A. GEE. *Med. J. Aust.*, **2**, 403–405. Sept. 10, 1955. 3 refs.

The symptoms and signs of pyelonephritis in pregnancy are so atypical that the diagnosis mainly rests on the presence in the urine of bacteria and pus, and on its differentiation from other fevers. Symptoms of the other common urinary diseases such as stone and hydronephrosis are so different from usual in pregnancy that they are readily masked by pyelonephritic manifestations. Sulphonamides are given 2 grammes daily in several weekly courses or over a long period. During pregnancy the prone position is best for drainage. Fluid intake should be 4 litres per day and the urine should be made alkaline by the ingestion of sodium bicarbonate. According to the sensitivity of the organisms antibiotics are given. Catheterization of ureters is now rarely necessary to drain the pelvis. If infection does not speedily clear, or if it recurs an excretion urogram should be taken. Too often this investigation is delayed until remedial measures cannot be undertaken.

The commonest factor causing persistent infection is calculous disease. At The Women's Hospital (Crown Street) over the past 5 years there have been at least 20

cases of calculous disease. This high figure is due to the alertness of the obstetrical staff in investigating persistent urinary infections and unexplained hypertension. Over the last 2 years the incidence of stones in the urinary tract in pregnancy has been once in every 600 confinements. They may be associated with hypertension which returns to normal after the removal of the stones.

In the surgical treatment during pregnancy open operation is usually only undertaken if there are major complications such as pyonephrosis.

Some patients have urinary tract dilatations prior to the pregnancy due mostly to aberrant vessels, strictures or hypoplasia. An excretion urogram makes the position clear.

S. Devenish Meares

93. **Urological Conditions in Pregnancy.**

By A. S. B. STUDDY. *Med. J. Aust.*, **2**, 400–403. Sept. 10, 1955. 7 refs.

Haematuria is more commonly seen in the later stage of pregnancy. It may be due to pyelonephritis, tuberculosis, hydronephrosis, polycystic disease, neoplasm or chronic nephritis. Urinary calculi do not often cause haematuria as dilatation of the upper part of the urinary tract is present. Haematuria in pregnancy should always be investigated. Bacteriuria occurs in about 11 per cent of pregnant women.

At the Royal North Shore Hospital of Sydney in the past two years only two cases of urolithiasis were detected. In pregnancy calculi are much more prone to be associated with infection, progressing to pyelonephritis and pyonephrosis. Obstruction is the main factor to be considered in urolithiasis. If there is no obstruction the calculus may be left until the pregnancy has been completed. If surgical intervention is necessary the calculus may be removed by percystoscopic methods or by lithotomy. Towards the end of pregnancy if surgical intervention is necessary a nephrostomy may temporarily relieve symptoms until a more radical operation can be performed.

The severity of a hydronephrosis depends on whether the condition is unilateral or bilateral and on the degree of infection present. More severe degrees of hydronephrosis ideally should be treated before pregnancy. If during pregnancy renal function deteriorates greatly termination may be necessary, followed by treatment of the hydronephrosis before another pregnancy is attempted.

Tuberculosis of the urinary tract is rare in association with pregnancy. After nephrectomy the state of the remaining kidney and the nature of the indication for the nephrectomy will determine whether a pregnancy should be allowed to continue or not.

Anuria may be due to mismatched transfusion, shock or haemorrhage, *Clostridium welchii* infection, and abortifacients. Conservative treatment rather than decapsulation or splanchnic block is best. It is important not to over-hydrate, and Bull and Joekes' method of management is favoured.

S. Devenish Meares

94. **Malignant Melanoma: Spontaneous Regression after Pregnancy.**

By E. P. ALLEN. *Brit. med. J.*, **2**, 1067. Oct. 29, 1955.

The case reported concerns a married white woman aged 38 who had had three children. In 1942 a tumour was excised from her right forearm. At that time it was thought to be a simple melanoma, but subsequent review showed it to be malignant. A local recurrence was excised in May, 1943 and malignancy was reported this time. A course of radiotherapy followed. Soon afterwards the patient became pregnant. In March, 1944, 10½ months after the second operation and when she was 28 weeks pregnant, she developed multiple subcutaneous bluish nodules on the left waist line, right flank and right upper arm. Biopsy from the latter site revealed a lymph node almost entirely replaced by tumour. In April a normal infant was delivered, and 14 days later the patient developed further deposits in the right scapula and inguinal regions. Three months later all the nodules, except for one groin gland, had disappeared. The patient had been seen periodically during the past 11 years and she has remained entirely well.

The author suggests that the metastases developed as a direct response to the stimulus of pregnancy and that they were so dependent on the stimulus that they disappeared upon its withdrawal. There was no local recurrence in the re-excised area and this raised the possibility that the "metastases" may have been multicentric foci of disease arising de novo, or that malignant cells lying dormant in the tissues had been activated by pregnancy.

R. W. Grayburn

LABOUR

95. **Physiopathology of Uterine Contractions.** (Fisiopatologiá de la contracción uterina.)

By B. SCHAFFER. *Obstet. Ginec. lat.-amer.*, **13**, 355–360. Sept. 1955. 20 refs.

Writers differ in their ideas about the physiology of the uterus, especially in regard to its behaviour at the onset of labour and during labour itself, and in consequence there is no generalized understanding of uterine dysfunction. The author therefore devised a clinico-therapeutic classification, which contains two main groups—major and minor.

The latter mainly comprises uterine inertia, for which he recommends the use of oxytocics. The former (major) group is described as consisting of those cases in which frequent contractions occur in the early phase of labour followed by either uterine exhaustion, tetany, Bandl's ring, etc. For the management of cases falling into this group, the author recommends careful labour ward observation including vaginal examinations, and the use of sedatives if necessary. He places surgical intervention high in the order of treatment, because he distrusts the influence of sedatives on the foetus. Indeed, for this reason, in normal cases, he injects a curare preparation into the perineum just before delivery and performs an episiotomy so as to minimize the intensity

of the uterine contractions, which he considers as an index of uterine dysfunction, maintaining that uterine contractions in normal labour should be painless.

John F. Foulkes

96. **The Place of Oxytocin in Labour.**

By D. LLEWELLYN-JONES. *Brit. med. J.*, **2**, 1364–1366. Dec. 3, 1955. 20 refs.

In this paper from the General Hospital, Kuala Lumpur, Malaya, the author discusses the use of intravenous pitocin in labour. He prefers a strength of 1 in 5,000 in dextrose, or dextrose saline, started at a rate of 20 drops per minute for 30 minutes, increasing by 10 drops a minute every half-hour to a maximum of 60 drops per minute until the pains are regular, lasting 30 to 60 seconds and recur every three to five minutes. If labour is satisfactory, the drip is continued until 12 hours have passed, or delivery occurs. If the result is not satisfactory at this concentration a 1 in 1,000 solution is substituted and given as before.

The author was satisfied that the pitocin drip was usually successful in initiating labour, if it had not begun 24 hours after amniotomy. He did not think it necessary to use it as a routine in all cases of amniotomy, but it was occasionally useful after amniotomy for antepartum haemorrhage. It was useful in inducing labour if it failed to start 24 hours after spontaneous rupture of the membranes. The method had proved safe and useful in cases of hypotonic uterine inertia.

There were two foetal deaths attributed to the pitocin drip in this series of 100 cases—one was due to contamination of the dextrose saline, with subsequent rigor. The second was due to too rapid administration of the drip, with intracranial haemorrhage. The author lists as contra-indications to its use: (1) Cephalo-pelvic disproportion. (2) Previous hysterotomy or Caesarean section. (3) Malpresentation. (4) Multiple pregnancy with much distension. (5) High multiparity.

Eileen Wilson

97. **Action of a Sympatheticolytic (Dihydroergotamine) on the Dynamics of the Uterus.** (Acción de un simpaticolítico (dihidroergotamina) sobre la dinámica uterina.)

By G. R. GIBELLI. *Obstet. Ginec. lat.-amer.*, **13**, 327–330. Aug. 1955.

A clinical investigation of the obstetric value of dihydroergotamine was made by the author upon 37 patients in the first stage of labour, 30 of whom were primigravidae. It was estimated that the cervix dilated more quickly in all cases, regardless of the state of the foetal membranes. In 33 of the cases the uterine contractions were increased in intensity and frequency. Delivery was spontaneous in 34 cases and 36 live babies were obtained. No harmful effect was noted on any foetus or mother. It is stated that in 22 cases, acceleration of dilatation of the cervix was increased between 4 and 36 times: in the absence of a control series, however, it is difficult to understand how this comparative estimate was made.

The author devotes the greater part of his paper to a discussion on the mechanism by which dihydroergotamine influences the dynamics of the uterus. Beginning with the observations of Sauter in 1948 using atropine and prostigmine, and subsequent experiments with acetyl-choline, he discusses the influence of the neuro-vegetative nucleus in maintaining the basal tone of the uterus, and the role of the sympathetic system in presiding over the contractile action. He admits however that the innervation of the uterus is complex, and refers to the old theory that the parasympathetic nerves are stimulators to the longitudinal muscle fibres of the uterine body and inhibitors to the circular fibres of the cervix—the sympathetic nerves having the opposite action. Thus the author maintains that stimulation of the neuro-vegetative nucleus produces impulses which are predominantly parasympathetic and at the same time are antagonistic to the sympathetic impulses.

When given in the first stage of labour, dihydroergotamine should be injected subcutaneously in doses of 0·25–0·5 mg., which may be repeated in 30 minutes, especially in the hypotensive uterus, in which its effect is most marked.

John F. Foulkes

98. **Ten Thousand Cases of Accelerated Labour.** (10,000 cas d'accouchement accéléré et indoloré.)

By N. C. LOUROS, N. BAROUS, N. ADAMIDÈS and S. HOULIS. *Gynéc. Obstét.*, **54**, 479–489. 1955. 11 tables.

The writers do not claim that they have introduced any new analgesic or oxytocic drugs, but state that the advantage of their technique is the combined administration of pethidine and an oxytocic in such a way as to accelerate labour and to render it infinitely less painful. This technique is only suitable for normal cases and is not used for patients with placenta praevia, eclampsia or disproportion. It is also best avoided in women with low blood pressure. The writers have found it particularly valuable in primary or secondary inertia, with either hyper- or hypotonic uteri, with ruptured or unruptured membranes. They have found it invaluable for elderly primigravidae.

At the onset of labour and at the beginning of cervical dilatation 50 mg. of pethidine is given intramuscularly. The progress of dilatation and the frequency of uterine contractions are carefully observed. If these are normal and pain is not relieved, a further 50 mg. is repeated in 15–30 minutes. This dose can be repeated if the pain continues. In many cases the labour will terminate without giving any oxytocic, but should it be required 1·5 to 2·5 international units of pitocin are employed in those cases where the frequency and power of the contractions diminish.

The *average* duration of labour has been markedly reduced by this method, and they found this to be 6 hours 15 minutes in primigravidae and 4 hours 35 minutes in multiparae.

The forceps rate was reduced from 6·1 per cent to 3·8 per cent and the incidence of craniotomy fell from 2·4 per cent to 0·31 per cent. Perineal tears were reduced from 21 per cent to 17 per cent.

The authors also found that pethidine had no ill effect

on the mother, and foetal anoxia was reduced to 1·1 per cent.

Pethidine is considered to be the best obstetric analgesic, and to have little, if any, effect on the foetus, provided it is used by experienced accoucheurs.

D. Maxwell

99. **Two Cases of Spontaneous Separation of the Cervix During Labour.** (Sobre dos casos de desprendimiento cervical espontaneo durante el trabajo de parto.)

By S. O. VALDANO. *Obstet. Ginec. lat.-amer.*, **13**, 190–195. July 1955. 1 illus. 12 refs.

The spontaneous separation of the cervix during labour is a rare occurrence. The first case of this nature was described by Scott in 1821, and up to 1933 only 17 such cases had been reported, but during the following ten years, the total increased to 54.

The first case reported by the author was that of a patient aged 28 years, para-1 plus 4. After a labour lasting 72 hours, the patient delivered herself, but immediately afterwards the midwife observed a fleshy mass in the vagina. This was found to be the cervix, which was attached to the uterus for about 2 cm. only. The cervix was removed and the patient made an uneventful recovery. The baby died on the 2nd day, and was found at autopsy to have a ruptured liver.

The second patient was a primigravida, whose cervix at 10 a.m. was 2-fingers dilated, and at 6 p.m. 4-fingers dilated; at 7.20 p.m. whilst pushing, she expelled the cervix followed by the foetus. The puerperium was normal in all respects, and the baby appeared none the worse for this unusual type of birth.

The first patient conceived again, but developed hydramnios and aborted at 6 months gestation.

John F. Foulkes

ANAESTHESIA

100. **Hypnotism in Pregnancy and Labour.**

By S. T. DELEE. *J. Amer. med. Ass.*, **159**, 750–754. Oct. 22, 1955. 12 refs.

The purpose of this article is to review the history of hypnotism in medicine and to evaluate its use in obstetrics. The author lists 13 advantages of hypnosis in obstetrics, and these are largely those of natural painless labour. The objections to hypnosis in general apply also in relation to obstetrics. In spite of the fact that 90 per cent of normal persons can be hypnotized to some degree, surgical anaesthesia can only be induced in about one out of four patients. It is also time-consuming although probably no more so than the preparation of patients for natural childbirth.

Prenatal training and conditioning is essential and this should begin about the third or fourth month of pregnancy. The patient should be hypnotized two or three times a month until the stage of deep hypnosis is reached, but if anaesthesia is not obtained after 10 sessions the outlook is poor. The hypnotic state is induced again at the onset of labour and the hypnotist's presence is necessary to prolong the trance and to prevent it from lapsing into natural sleep from which the patient could awaken with actual distress. Operative procedures can be carried out under hypnosis alone, but during spontaneous delivery some participation by the mother can be effected upon command. Although the true mechanism of hypnosis has not been explained, its applications are growing daily, and if judiciously employed it is proving a powerful ally in relieving many functional conditions in obstetrics and gynaecology.

D. W. James

101. **Role of Dolantin in Cervical Dilatation and Anaesthesia During Intrauterine Intervention.**

By E. SZIRMAI and G. SILLO. *Ann. chir. gynaec. fenn.*, **44**, 108–115. 1955. 2 figs. 22 refs.

Dolantin in 50 mg. doses by mouth reduces the pain and increases the rapidity of labour. In 33 cases of artificial induction of abortion and dilatation of cervix for curettage Dolantin was given. In 16 cases, 100 mg. was injected into the cervix and the remainder intramuscularly. As a result, cervical dilatation was accomplished easily and painlessly. Its action appears to be particularly on the lower uterine segment. Dolantin reduces muscle fatigue in the extremities as recorded by the Szirmai myotonograph and myotonometer.

[This report is from Hungary and one would presume from it that anaesthesia is not used for dilatation of the cervix.]

D. M. Sheppard

PUERPERIUM

102. **X-ray Treatment of Puerperal Mastitis.** (La roentgenterapia delle mastiti puerperali.)

By ROSSI, RABAIOTTI and BOCCHIALINI. *Minerva ginec., Torino*, **7**, 669–672. Oct. 15, 1955. 3 graphs. 20 refs.

The author complains that though the medical and surgical treatment of puerperal mastitis is well understood and widely practised, treatment by roentgen therapy is either unknown or, even worse, viewed with scepticism and mistrust. Puerperal mastitis is an acute or subacute inflammatory process due to infection through the milk ducts or through cracks and abrasions of the nipple area. Three stages are recognizable: (1) hyperaemic congestion with lymphangitis accompanied by a slight fever; (2) to increased redness, heat and pain are added induration, commencing oedema, a feeling of tension and a well-defined rise of temperature; and (3) suppuration shown by an area of fluctuation in the affected area. Left untreated, suppurating fistulae widely invade the breast tissue.

Radiation treatment is indicated in each phase though the clinical course is different according to the clinical phase present when treatment is started. After a discussion of the mode of action of roentgen therapy, details of its application are given. The area treated must be wide and must include the nipple area. Dosage should be proportionate to the acuteness of the inflammatory process, normally 80r at a sitting, repeated in 48 hours if required. Radiation hardness of 140–160 filtered by

5 mm. of aluminium or 0·5 of copper, focal distance 40 cm. is suggested.

In the early stage obvious relief is obtained in a few hours, leading to rapid resolution of the inflammatory process. In later stages, relief from pain is soon noticed, and a general improvement of the patient's condition, both subjective and objective, is seen, though a second or even a third treatment may be necessary to complete the resolution. In the stage of suppuration, this process is localized and limited so that surgical intervention is simplified; in most cases aspiration is all that is needed. The authors review 100 cases treated in this way with examples, the majority in the earlier stages, and claim that the method is extremely efficient, and commend it strongly to notice.

W. C. Spackman

103. **Disturbances of the Late Puerperium.**

By Axsel Saloheimo. *Ann. chir. gynaec. fenn.*, **44**, 195–202. 1955. 23 refs.

Two hundred mothers were examined at postnatal clinic 6–8 weeks post-partum. Forty-five per cent complained of backache, caused by a variety of lesions from constipation to parametritis. Lactation was adequate in 50 per cent, and 23 per cent had had their first period. 43·5 per cent resumed coitus within six weeks of delivery. 1·5 per cent showed persistent albuminuria and 19 per cent had mild anaemia.

The author stresses the importance of postnatal examination as apparently only 7·7 per cent of all deliveries in Finland attend postnatal clinics.

D. M. Sheppard

104. **Anticoagulant Treatment with Phenylindanedione in Obstetrics and Gynaecology.** (Il trattamente anticoagulante con fenilindandione in ostetricia e ginecologia.)

By F. Malagoli. *Ann. Ostet. Ginec.*, **77**, 403. Apr. 1955. 11 refs.

The treatment of 18 cases of puerperal and post-operative phlebothrombosis is described; 10 received the anticoagulant phenylindanedione alone, while the remaining 8 received heparin and phenylindanedione.

Phenylindanedione, which has a pharmacological action similar to that of dicoumarin, is found to be an excellent anticoagulant. The period of latency is 24–48 hours, less than that of dicoumarin. The effect in maintaining a low level of prothrombin activity is well sustained but flexible. It is easily neutralized by administration of vitamin K_1 by mouth. Toxicity is low, even with prolonged administration, and the clinical effects have been found to be excellent.

When heparin is used in association with phenylindanedione, a rapid effect is obtained and heparin may be used during the latent period of phenylindanedione.

[Phenylindanedione is well known in this country as a reliable anticoagulant and is often known by the proprietary name of "Dindevan".]

Josephine Barnes

INFANT

105. **The Diagnosis of Sex Before Birth Using Cells from the Amniotic Fluid.**

By D. M. Serr, L. Sachs and M. Danon. *Bull. res. Coun. Israel*, **5B**, 137–138. 1955. 6 figs. 12 refs.

This preliminary report comes from the Hadrassah University Hospital and the Weizmann Institute of Science. Amniotic fluid was obtained by puncture of the membranes shortly before delivery. After centrifuging the fluid, the cells in it were smeared on slides, fixed in alcohol-ether, and stained with Feulgren and fast green. In 20 such cases it was possible to determine the foetal sex correctly by observation of the percentage of cases with chromocentres, especially those at the nuclear membrane. Fluid may also be obtained by paracentesis, and it has been found that cells suitable for diagnosis can be obtained at the fifth month of pregnancy.

S. G. Clayton

106. **Hyaline Membrane and Foetal Aspiration Syndromes.**

By H. G. Peterson, Jr., and M. E. Pendleton. *Amer. J. Roentgenol.*, **74**, 800–817. Nov. 1955. 2 tables. 2 charts. 9 figs. 17 refs.

Hyaline membrane disease is a common cause of sickness and death in the newborn and the present study was undertaken to evaluate roentgenographic examination in diagnosis and treatment. One hundred and forty-seven infants having respiratory distress were studied, of which 138 showed one of two different and distinct abnormal patterns. The most commonly encountered picture (104 infants) was one of abnormal aeration, characterized as finely reticulogranular with a general increase in lung density of uniform distribution. The second, less common, roentgenographic picture (34 cases) showed a more irregular and coarse appearance with focal areas of uneven aeration, some appearing emphysematous and others atelectatic or consolidated. When these changes were marked, the chest had a hyperexpanded appearance with elevation of the upper anterior ribs above the levels of the corresponding portions, giving the rib-cage a crablike appearance. One impressive feature in favourable cases was the rapid and substantial clearing of the lung picture within 12–24 hours.

Of the 104 infants presenting the reticulo-granular pattern, 77 were premature, 55 born by Caesarean section and 31 were complicated by placental abnormalities. Only 9 of the group were full term normal deliveries. In general, there was good correlation between the severity and duration of the respiratory distress on the one hand and the lung density and persistence of roentgenographic changes on the other. Twenty-three infants died within the period of initial illness, all having heavy lungs which sank in water and on microscopy showed generally distributed hyaline membrane within the terminal bronchioles, alveolar ducts and some alveoli. Widespread resorption atelectasis of alveoli was often present, and in 9 infants who lived 30 hours or more there was

moderate to marked inflammatory infiltration. Of 3 infants dying after apparent clinical improvement, 1 died two days later showing a marked macrophage response throughout the lungs with multiple liver abscesses, another died 4 days later with haemorrhagic infarction of the adrenal glands and a marked pulmonary macrophage response, and the third died 10 days later with an extensive pneumonia and pulmonary abscess formation.

Of 34 infants showing the coarse irregular pattern, none were premature but 21 were postmature. Foetal distress during labour was not uncommon and rapid clinical improvement correlated well with substantial clearing of the lung picture in the first 12 to 24 hours. Four infants in this group came to autopsy, the lungs being crepitant and tending to float. Microscopy showed gross aspiration of keratinized squamous cells, some meconium, focal alveolar emphysema and atelectasis. The findings in both groups suggest that the radiologist is in a position to indicate the basic processes involved in respiratory distress in the newborn and to rule out gross congenital abnormality such as massive diaphragmatic hernia. Improvement is often apparent radiologically before any change in the physical state. The exceptional correlation of the radiological and clinical patterns establishes roentgenographic examination to be a valuable diagnostic aid in the care and study of newborn infants with respiratory distress.

John H. Mulvany

107. **Anoxia as it Affects the Foetus and New-Born Infant.** (Sindrome anossica fetoneonatale.)

By E. FERRARIO. *Minerva ginec., Torino*, **7**, 643–656. Oct. 15, 1955. 14 graphs. 8 tables. 73 refs.

Relative lack of oxygen before and during birth is almost certainly the principal cause of perinatal mortality of otherwise healthy infants and may well be responsible for permanent damage in the survivors. In an endeavour to sort out the principal causes of foetal distress or neonatal death due to anoxia the author investigated 122 cases of foetal distress seen at the Obstetrical School of Novara. Of these, in 31 no specific cause could be apportioned, in 50 some single factor could be indicted, and in 41 two or more factors appeared to operate. As single causes, the list includes 13 items such as postmaturity, prolonged labour, malpresentations, abnormalities of the cord, forceps, elderly primiparity. Placenta praevia and premature separation of the placenta, though mentioned elsewhere in the paper, are not mentioned in the case list which also omits prematures, twins, foetal malformations, Caesareans and stillbirths as well as foetal anoxia due to drugs and anaesthetics administered to the mother. Of the 122 babies considered, 12 died neonatally and 9 showed signs of intracranial haemorrhages confirmed by rachicentesis. Where more than one cause is indicted, postmaturity figures in a large proportion; it is usually accepted that the combination of placental senescence, increasing foetal requirement of oxygen and decreased plasticity of the foetal head (leading to prolonged labour) operate in this serious complication.

The conclusion reached is that in view of the large number of factors involved in producing or contributing to the anoxic syndrome an improvement in the outlook and statistics cannot be looked for without close co-operation between the antenatal supervisor, the accoucheur and anaesthetist, and the paediatrician.

W. C. Spackman

108. **Retinopathy in Premature Infants (Retrolental Fibroplasia).** (Le drame de la rétinopathie des prématurés (fibroplasie rétrolentale).)

By J. ZANAN. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 233–246. 1955. 14 figs.

This disease, discovered and identified by Terry, chiefly affects small premature babies after birth. The final stage of the disease, that of retrolental fibroplasia, originally gave its name to the disease, but subsequently earlier stages have been observed and disclose the primary vascular abnormality. At a later date clinical tests incriminated a little-suspected cause for the retinopathy, namely excessive oxygen supply.

The author, in collaboration with Doctors Meunier and Piraux, investigated the concentration of oxygen actually present in incubators. When the concentration of oxygen in the incubators was kept below the amount theoretically given they no longer found cases of retinopathy.

Further studies, namely those of Ashton, Ward and Serpell, proved the vaso-constrictor role of oxygen on the retina of man and animals.

From the Author's Summary

109. **Retinal Haemorrhage in the Newborn Full-term Infant.** (A propos des hémorragies rétiniennes du nouveau-né à terme.)

By E. CAVROT. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 247–263. 1955. 21 refs.

Retinal haemorrhage is a common but harmless affection found in 33 to 42 per cent of full term babies. Nevertheless it is a reliable sign of vascular injury, due to stress during labour. It may be due to capillary fragility, or obstetrical factors leading to foetal injury or anoxia.

A statistical study of the influence of different obstetrical conditions is presented (421 cases). The frequency of retinal haemorrhage can be reduced by from 3 to 5 times (to 7 per cent) by prenatal administration to the mother of a non-toxic complex of substances which improve the vascular fragility, provided that it is given for at least the last 5 weeks.

These observations indicate the risk of cerebro-meningeal bleeding, because both that and retinal haemorrhage are connected with vascular resistance.

From the Author's Summary

110. **Ophthalmia Neonatorum.** (Ophtalmie des nouveau-nés.)

By P. DUMONT and M. DE HAZE. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 212–225. 1955. 1 fig. 6 tables. 77 refs.

Today the majority of infections of the conjunctivae of the new-born are caused by staphylococci. The gonococcus is rarely found in countries with high hygienic standards.

A comparison is made between Silver Nitrate and

Argyrol as prophylactics. Among 5,437 cases treated with silver nitrate (1·5 per cent) conjunctivitis occurred in 6·8 per cent, including reactions attributed to the silver nitrate. There was no gonococcal case. Among 5,460 cases treated with argyrol (5 per cent) conjunctivitis occurred in 2·1 per cent. The cases of conjunctivitis in the second group more frequently required intensive treatment with penicillin.

Many authors are in favour of using an antibiotic (penicillin or aureomycin) or sulphonamides for prophylaxis. Their results appear to be favourable, and it is proposed to risk a trial of these.

From the Authors' Summary

111. **Early Diagnosis of Atresia of the Oesophagus.** (Contribution au diagnostic précoce de l'atrésie oesophagienne.)

By P. Cieters and R. de Rom. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 294–302. 1955. 3 figs. 16 refs.

In 50 per cent of cases of oesophageal atresia in the newborn surgery can be successful. Early diagnosis is essential to prevent attempts at feeding with subsequent complications, and also so that surgery can be done earlier and in better conditions. Although there are no characteristic early signs during the first hours of life, hydramnios is usually present and should make the obstetrician suspect this diagnosis, which can be confirmed by passing an oesophageal tube.

From the Authors' Summary

112. **The Influence of Virus Infections in Pregnancy on Congenital Malformation.** (Les effects malformatifs chez l'enfant des infections virales de la mère.)

By J. François and G. Verriest. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 182–211. 1955. 4 figs. 265 refs.

The embryopathy of rubella is characterized by congenital malformations which occur (*a*) in the eye, as central or total cataract, microphthalmia, or dystrophy of the retina, (*b*) in the inner ear, as complete or partial deafness, or labyrinthine abnormalities, (*c*) in the heart, involving the arterial duct or interauricular septum. Cranio-cerebral, dental or somatic anomalies are rare. Typically, two anomalies are associated, either ocular anomalies or deafness with congenital heart disease. Cataract is only rarely found with deafness, because the lens develops at a different time (second month) from the inner ear (third month).

If the mother has rubella during the first trimester of pregnancy abortion or stillbirth may occur, or the foetus may show an embryopathy. The percentage of affected children varies from 10 to 50 per cent in different epidemics, depending on the virulence of the virus.

The malformations are probably due to the direct action of the virus or its toxins on the developing organs. Treatment must be preventive by immunizing the mother by infecting her before pregnancy, or by injections of convalescent serum during the period of incubation.

Other virus infections can cause foetal abnormalities, especially epidemic parotitis, smallpox, poliomyelitis and epidemic hepatitis.

From the Authors' Summary

113. **Evaluation of Perinatal Deaths.**

By P. Gruenwald. *Obstet. Gynec.*, **6**, 471–481. Nov. 1955. 35 refs.

The pathological findings at post-mortem in the perinatal period make statistical evaluation of the causes of death both difficult and complex. They do not necessarily reveal the cause of the death. The author believes that a system as simple and inclusive as that presented by many who write on the subject cannot satisfy all criteria of sound evaluation. For example, prematurity is used to designate a cause of death by some authors and not by others. Asphyxia or anoxia is used in statistics by various authors in many different ways, and the same applies to atelectasis. Aspiration of amniotic fluid is presumably a normal occurrence, but not necessarily aspiration of vernix caseosa or meconium. A peculiar mononuclear pneumonia frequently unassociated with bacterial infection is found in some infants dying after 1 week. The aetiology of this condition is obscure.

The author believes that the following directions may aid in avoiding serious errors:

1. Pathological findings should be classified separately from and independently of the patient's history. A diagnosis based on pathological findings differs in significance from the same diagnosis based on clinical observation.

2. The causes of perinatal distress should be separated from its sequelae. The ultimate cause of death may differ from the underlying one.

3. Cases with no significant findings at autopsy should be separated from those in which no autopsy was done. It should be remembered that anoxia or trauma may have been present without leaving detectable signs.

4. Although prematurity plays an important role it is not strictly comparable with other causes of death.

J. G. Dumoulin

114. **Suppurative Lymphadenitis Following Intradermal B.C.G. Vaccination of the Newborn.**

By J. Guld, K. Magnus, K. Tolderlund, K. Biering-Sørensen and P. Q. Edwards. *Brit. med. J.*, **2**, 1048–1054. Oct. 29, 1955. 6 figs. 9 refs.

This is a preliminary report which comes from Copenhagen. The object of the investigation was not only to study the frequency and severity of glandular involvement following the use of B.C.G. but also to discover the relation between the dose of vaccine and the degree of B.C.G.-induced tuberculin sensitivity in newborn infants.

A total of 1,513 babies were vaccinated between 1 and 11 days after birth without preliminary tuberculin tests. B.C.G. was injected into one or both deltoid regions in six different total doses ranging from 0·15 to 0·0047 mg. The one-year follow up period is not yet complete.

There was no doubt that the larger the dose of B.C.G., the greater the likelihood of lymph node involvement. Twenty-five per cent of the babies had enlarged or perforated nodes after a dose of 0·15 mg., whereas only occasional involvement occurred when the weaker doses were used, and yet the degree of post-vaccination tuberculin sensitivity was relatively little affected.

Little advantage was found in giving the total dose of B.C.G. in two injections, one in each shoulder, rather than in a single injection. In fact, babies given two injections developed more than twice as many complications as those receiving only one injection.

B.C.G. used 12 days after harvest caused slightly fewer complications than that used 5 days after harvest but the incidence of allergy seemed to be the same.

R. W. Grayburn

MATERNAL MORTALITY

115. **The Causes and Prevention of Maternal Mortality.** By R. J. KELLAR. *J. Irish med. Ass.*, **37**, 269. Sept. 1955. 1 ref.

In this paper Professor Kellar deals with the maternal deaths which occurred in Scotland during the period 1949 to 1954. During the six year period there was a steady fall in the number of maternal deaths until, in 1954, the incidence was 0·7 per 1,000 live births. This represented 70 maternal deaths in 1954.

Professor Kellar had had the opportunity of studying many of the case notes of the mothers who died. The causes of death are enumerated and discussed. After a study of the available information, Professor Kellar is of the opinion that really good and intelligent antenatal care would do much to reduce the number of mothers who lose their lives in childbirth but the support of a hospital flying squad is essential. Although post-partum haemorrhage is generally regarded as being a preventable cause of maternal death no fewer than 66 women lost their lives from this complication during the 6 year period. The majority of these deaths occurred in domiciliary practice, in private nursing homes or in small hospitals. Most were delivered outside an established maternity hospital.

[Professor Kellar gives much factual information of interest in this paper and does not hesitate to set down his own personal views.]

J. K. Russell

OBSTETRIC OPERATIONS

116. **Caesarean Section—Indications.** By L. TOWNSEND. *Med. J. Aust.*, **2**, 256–259. Aug. 13, 1955.

At the Royal Women's Hospital, Melbourne, there are now 7,000 deliveries each year, including 250 Caesarean sections. The maternal mortality associated with the operation is less than 1 per cent.

During the last 3 years 665 patients were delivered by Caesarean section, 206 of these being repeat operations. Cephalo-pelvic disproportion was the commonest indication. It was the indication in 226 patients, 108 of whom were having the operation repeated. In the management of cephalo-pelvic disproportion of intermediate degree a trial of labour was given. It was not the aim to achieve a vaginal delivery at all costs, but on the other hand elective Caesarean section was not undertaken except in the most severe types of disproportion.

Sixty-one per cent of patients with placenta praevia were delivered by Caesarean section; this amounted to 104 patients. In this group there was no maternal death and a foetal wastage of 18 per cent.

In 39 cases malpresentation was the indication. Thirty-one patients underwent Caesarean section for pre-eclampsia. During the 3 years there were 72 cases of eclampsia, and 4 of these were delivered by section. In 27 patients the indication was prolapse of the cord, with a cervix not sufficiently dilated for vaginal delivery. Failure to induce labour by artificial rupture of the membranes was the indication in 20 cases. Abnormal uterine action was the cause of 18 Caesarean deliveries.

In the remaining cases the indications in order of frequency were diabetes, essential hypertension, previous vaginal repair, placental insufficiency, fibroids, previous dystocia, intractable vomiting, previous hysterotomy, failed forceps, together with 23 miscellaneous indications.

Of the 297 patients with a history of previous Caesarean section 88 were delivered vaginally. In the group of those who had elective Caesarean sections there were four patients in whom the uterus had ruptured.

The contra-indications to Caesarean section are eclampsia, accidental haemorrhage, death of the foetus and monsters, unless there is a placenta praevia of type iii or iv. Lower segment Caesarean section is the operation of choice, the classical operation being indicated when there is a transverse lie which cannot be corrected and when there is a constriction ring.

There were 4 maternal deaths in the series of 665 sections with a foetal wastage of 148 per 1,000.

S. Devenish Meares

117. **Afibrinogenaemia Associated with Severe Uterine Haemorrhage Following Caesarean Section.** By N. KIMBALL and A. K. GHOSH. *Lancet*, **1**, 82. Jan. 14, 1956. 4 refs.

The authors report a case of afibrinogenaemia. The patient was admitted as an emergency for prolapsed cord. Lower segment Caesarean section was performed. Haemostasis was difficult to achieve and some blood was taken for cross-matching. It was found that this blood did not clot over a period of time, and the patient was treated with triple-strength plasma and later with fibrinogen intravenously followed by blood-transfusion.

H. H. Fouracre Barns

GYNAECOLOGY

118. **Vaginal Length and Uterine Position.** By A. B. CHIDESTER. *Obstet. Gynec.*, **6**, 516–518. Nov. 1955. 17 refs.

In patients with retroverted uteri, the average length of the anterior vaginal wall was estimated by the author as 7·11 cm. and of the posterior wall 9·84 cm. In individuals with an anteverted uterus, the anterior wall measured 9·4 cm. and the posterior 11·55 cm.

The author considers that retroversion of the uterus is caused or aided by a short anterior vaginal wall. It is an

anatomical condition which is not abnormal for the individual in whom it occurs.

J. G. Dumoulin

119. **Classification and Treatment of Various Congenital Malformations of the Uterus and Vagina.** (Fisionomia clinica e trattamento di alcuni particolari tipi di malconformazioni congenite utero-vaginali.)

By P. N. Siliquini and G. Pinoli. *Minerva ginec., Torino*, **7**, 699–709. Oct. 31, 1955. 10 figs. 110 refs.

These cases fall into four main groups: (1) young girls with monthly pain but no menstrual loss, (2) young women with normal external genitalia and sex desires who wish to marry but are aware of some impediment to normal intercourse, (3) women without sex impulses or menstruation who consult a doctor because they realize their condition is abnormal, and (4) women who after perhaps years of marriage feel a desire to be able to have normal intercourse.

Clinical investigation is not difficult, but due regard must be given to tactful handling of young and sensitive patients. The means involved are bimanual and speculum examinations; radiological investigations with and without concurrent visualization of the urethra, bladder and rectum; coelioscopy, and exploratory laparotomy.

The paper discusses the abnormal developmental processes producing the various defects, gives three detailed cases and discusses a variety of operative procedures which can appropriately be carried out, especially as regards the provision of an artificial vagina.

W. C. Spackman

120. **Fifty Cases of "Pelipathia vegetative spastica".** (50 Fälle von Pelipathia vegetativa spastica.)

By U. Müller. *Gynaecologia, Basel*, **140**, 129–140. Sept. 1955. 5 tables. 23 refs.

The polysymptomatic picture of functional disorder of the female pelvic organs was named by Gauss (*Dtsch. med. Wschr.*, 1949, **74**, 1288) pelipathia vegetative spastica, though the syndrome had already received over 30 different names. The syndrome is described as existing in a spastic and a congestive form; the present investigation deals with the former variety.

The outstanding symptom is pelvic pain often worse before and after menstruation. Irregularity of the cycle is common. Dyspareunia and disorders of libido are frequent. Abortion and sterility are not uncommon. This syndrome is frequently associated with psychological disorder. Objective physical signs in the pelvic organs are unusual; often there is hypersensitivity of the genitalia with vaginismus on examination, but the uterus and adnexa seem normal on palpation. Leucorrhoea may be present but curettage reveals normal endometrium. General nervous symptoms are common and the body temperature is often subnormal. Various neurotic symptoms are present, mainly in the form of emotional immaturity and mother fixation. Suicidal tendencies may be noted. Differential diagnosis is from organic disease such as salpingitis, tuberculosis, appendicitis, diverticulitis, neoplasm and endometriosis.

A description is given of 50 such cases, collected from 2,500 gynaecological cases. Treatment is psychiatric, and attempts to loosen the rigid isolation in which these patients tend to live.

In summing up the author emphasizes the essential loneliness of these patients who tend to isolate themselves. Marital conflicts, divorce, a low birth rate and frequent miscarriages are further evidence of their unsuccessful adaptation to society.

Josephine Barnes

121. **X-ray Diagnosis in Metrorrhagia. A Study of 706 Cases.** (Le diagnostic radiologique des métrorragies. Etude portant sur 706 observations.)

By J. Dalsace, — Guilloux, — Kramarz and — Melamed. *Gynéc. Obstét.*, **54**, 473–478. 1955. 2 tables.

Following the work of Béclère the writers carry out hysterosalpingography in cases of metrorrhagia whenever the diagnosis is uncertain.

Out of 2,500 hysterosalpingographies carried out since 1927 they have extracted 750 cases in which there was metrorrhagia. They only retained those which were followed up personally or by questionnaire and these finally numbered 706.

Of these 706 cases 487 occurred prior to the menopause; made up of 321 cases with surgical lesions such as fibroids, polyps, carcinoma of body and cervix, etc., and 106 functional metrorrhagias.

Post-menopausal cases numbered 219: there were 78 cases of malignant disease of the corpus and 4 of cervical cancer. There were 137 benign lesions, 75 of which were diagnosed as functional metrorrhagia or undiagnosed.

They conclude that the results of hysterosalpingography in these cases entirely overthrow the classical teaching of the past. Cancer of the corpus frequently occurs prior to the menopause, often encroaches beyond the region of the isthmus, and not infrequently co-exists with other cancerous lesions of the genital tract. After the menopause uterine cancer is not the commonest cause of bleeding.

About two-thirds of the cases in women of childbearing age are functional. Hysterosalpingography demonstrates the danger of indiscreet oestrogen therapy in menopausal women.

D. Maxwell

122. **Hormonal Treatment of Functional Uterine Haemorrhage.** (Nos expériences dans le traitement hormonal des hémorragies fonctionnelles.)

By K. G. Ober. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 303–319. 1955. 10 figs. 33 refs.

The aetiology of so-called functional bleeding is established by clinical and experimental observations. Eighty per cent of the cases are due to long-persisting oestrogen secretion, without ovulation and hence no corpus luteum formation. Bleeding from a mucosa in involution with secretory changes may be due to an early abortion which has not been detected by clinical investigation. Such cases may be included in the func-

tional bleeding group, and account for up to 20 per cent of the cases.

It is still impossible to be certain of inducing ovulation by treatment. In order to treat functional haemorrhage the lacking corpus luteum hormone must be replaced by artificial hormones. The corpus luteum produces in 12 to 14 days about 200 mg. of progesterone and oestrogens equivalent to 10 mg. of oestradiol. Long-acting preparations are convenient. A crystalline suspension was made containing 200 mg. of progesterone and 10 mg. of oestradiol benzoate, with a 14 day action.

Three hundred and thirteen unselected cases with the clinical picture of functional bleeding were given one injection of this suspension. Twenty-six did not respond, i.e., the haemostasis and subsequent endometrial shedding ("hormonal curettage") did not occur. It was found later that in 23 cases the bleeding had another cause.

It may be that in the future hormonal treatment will replace the treatment of functional bleeding by repeated curettage, especially in young girls and women of child-bearing age.

From the Author's Summary

123. **Time Required for the Action of Progesterone on the Endometrium in Ovariectomized Women.** (Vitesse d'apparition des premiers critères endométriaux de l'action progestéronique chez la femme ovariectomisée.)

By J. FERIN, J. BONTE and J. V. VASSILOPOULOS. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 265–271. 1955. 5 figs. 8 refs.

After preliminary treatment with oestrogens an ovariectomized woman was given 100 mg. of progesterone by intravenous drip, continued for 14 hours. After 6 hours some glycogen droplets appeared at the base of some of the cells in a few endometrial glands, and at the same time there was a marked increase in the alkaline phosphatase content. After 14 hours basal glycogen deposits were found in the majority of the glands, but the phosphatase did not increase further. There were no evident changes in the vaginal smear.

The endometrial content of alkaline phosphatase depends on an oestrogen-progesterone mechanism, and may have some relation to glycogen storage.

From the Authors' Summary

124. **Leucoplasia of the Cervix.** (Les leucoplasies du col.)

By R. BORY and M. JAMES. *Gynéc. Obstét.*, **54**, 464–472. 1955. 3 figs.

The term leucoplasia of the cervix is badly chosen, and the writers would prefer to substitute the word leuco-keratosis. It is a complex process, the place of which in the classification of diseases is not defined; only its anatomo-pathological criteria are well established. In the writers' personal statistics 10 per cent of the leucoplasias studied were accompanied by an epithelioma.

In their opinion the discovery of a leucoplasia always calls for a biopsy in order to verify the histological diagnosis as such cases are potentially malignant. Benign leucoplasia warrants active therapy aimed at its complete destruction. Electro-coagulation in the writers' hands, provided it is carried out with meticulous care, following a special technique has resulted in 90 per cent of their cases returning to normal.

D. Maxwell

125. **Life History of the Human Testis.**

By E. T. ENGLE. *J. Urol.*, **74**, 379–386. Sept. 1955.

As a result of McLeod's work on semen analysis we now have standards of male fertility. Testicular biopsy is a most useful aid and a necessary one in many cases of subfertility. There is no cure for azoospermia due to germinal aplasia, and the outlook for oligospermia with progressive tubular fibrosis is bad. In oligospermia with no fibrosis a metabolic defect is the probable cause. The treatment of oligospermia by testosterone, gonadotrophins and shotgun therapy of vitamins, minerals and thyroid extract are of no avail. Perhaps hope of future progress lies in understanding the metabolism of the cells during the various stages of spermatogenesis and the mode of action of the gonadotrophins and steroids under enzymatic influence.

J. H. Carver

INFECTIONS OF THE REPRODUCTIVE ORGANS

126. **Antibiotic Therapy of Tuberculosis of the Female Genitalia.**

By I. HALBRECHT. *Lancet*, **2**, 1165–1167. Dec. 3. 1955. 5 tables. 7 refs.

The author records his results of treatment of female genital tuberculosis with streptomycin and *p*-amino-salicylic acid. There were 74 patients treated and of these 21 were considered to have tubal, 49 endometrial and 4 exudative tuberculosis. The differentiation between tubal and endometrial tuberculosis was apparently made on obtaining a positive culture from menstrual and inter-menstrual discharges but a negative endometrial biopsy. Sixty-eight of the 74 patients received the full treatment of 45 grams of streptomycin, which was considered to be the minimum needed for cure. In 48 of these 74 patients no signs of genital tuberculosis could be discovered from one to six years after the treatment, whereas recurrences occurred in the remaining 26 patients. Out of 49 patients treated for endometrial tuberculosis 16 had recurrence of the genital tuberculosis. In the 4 cases of exudative tuberculosis, there were adnexal tumours clinically and the diagnosis of tuberculosis was confirmed by positive cultures of the menstrual discharges. These patients received a higher dosage of treatment but in spite of this there was a positive culture of the menstrual discharges within 6–18 months after treatment.

Seven ectopic and 5 intra-uterine pregnancies followed upon the antibiotic treatment in the 74 patients. Three of the 5 intra-uterine pregnancies resulted in full term healthy babies and the other two ended in abortion.

The author concludes that healing of the female genital tuberculosis cannot be considered definite until at least 3 years has elapsed since the start of treatment.

H. H. Fouracre Barns

127. **Control of Chronic Lower Genital Tract Infections.** By C. E. FOLSOME, S. A. LESLIE and R. K. THOMS. *Obstet. Gynec.*, **6**, 532–537. Nov. 1955. 2 refs.

An acidic ion-exchange resin treated with sodium hydroxide to elevate its initial pH to 2·2–3·5, made into a tablet called Vacid, was used in 113 cases exhibiting variable grades of subacute cervico-vaginitis. Five hundred mg. of the resin inserted into the vagina once daily for 2 weeks maintained a vaginal pH level of 3·5–5·0, and proved effective treatment in all cases. It also was successful in destroying trichomonal infestations.

J. G. Dumoulin

128. **Treatment of Inflammatory Diseases of the Female Pelvic Organs with Presacral Novocaine Blockade.** By N. P. VERKHATSKII and L. T. LAPA. *Sov. Med.*, **9**, 61–62. Sept. 1955.

The remarkable effects of novocaine blockade in assisting the resolution of inflammation in the female genital organs are here described. The method is based on the teaching of I. P. Pavlov on the trophic function of the nervous system, and was tried on 85 acute and subacute cases and on 70 chronic cases of female genital sepsis. From 80 to 120 ml. of 0·25 per cent novocaine was injected through a needle inserted between the anus and coccyx to a depth of 2–3 cm. in the direction of the anterior surface of the sacrum, with the patient in the lithotomy position. The injections were given at intervals of 3–4 days; 10 of the patients received only one injection, 48 two, 76 three, 13 four, and 2 five.

Of the 85 acute cases, 45 fully recovered, 22 were much improved, 8 slightly improved, 8 received no benefit and 2 were worse. Of the 70 chronic cases, 28 made a full recovery, 16 partial recovery, 17 showed slight improvement, 8 no effect and 1 was worse.

No other treatment is mentioned, and the patients were ambulant. The results were assessed on general well-being, temperature, diminution or disappearance of inflammatory swelling and infiltration, blood picture, E.S.R., and in 50 cases on the electrical conductivity of the skin. It was found that 35 acute cases of pelvic inflammation showed an increased conductivity in the skin zones of Snegerev and Lapinskii, which fell to normal with the subsidence of the inflammatory process; in chronic cases this increase of skin conductivity was not observed.

L. Firman-Edwards

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

129. **A Contribution to the Study of Malignant Mesenchymal Tumours of the Female Genital Tract.** (Contributo allo studio dei tumori mesenchymali maligni dell'apparate genitale femminile.) By M. ZORZI and G. CALLEGARI. *Ann. Ostet. Ginec.*, **77**, 414. Apr. 1955. 34 refs.

Three rare mesenchymal tumours of the female genital tract are described. The first was a lymphosarcoma of the portio vaginalis of the cervix. This occurred in a woman of 57. The patient died with intra-abdominal secondaries, arising mainly by lymphatic spread.

The second tumour was a leiomyoblastoma of the Fallopian tube. This was found at operation in a woman aged 23. The patient subsequently died of secondaries but no autopsy was obtained.

The third tumour was a fibrosarcoma of the ovary, discovered at operation in a woman aged 54. The histological picture was that of a fibrosarcoma of the ovary though at operation the tumour presented as partly cystic. The diagnosis from the different varieties of granulosa-cell tumour, arrhenoblastoma and disgerminoma are discussed.

Josephine Barnes

130. **Vascular Tumours of the Female Genital Tract.** By A. B. GERBIE, M. R. HIRSCH and R. R. GREENE. *Obstet. Gynec.*, **6**, 499–507. Nov. 1955. 74 refs.

Hemangiomas of the Uterine Cervix. By R. T. BRANDFASS and L. C. SCHEFFEY. *Obstet. Gynec.*, **6**, 508–510. Nov. 1955. 9 refs.

Vascular tumours of the female genitalia are not common. Haemangiomas are benign tumours of the blood vessels. Usually they are asymptomatic and may be small. They rarely are found on the vulva and cervix. More commonly they are found in the uterine corpus where they are usually asymptomatic, and rarely they have been reported in the round ligament, the tube and the ovary. The authors present 5 cases, 1 in the cervix, 3 in the myometrium and 1 in the ovary.

Lymphangiomas are similar to capillary haemangiomas except they contain no blood cells, and they occur in the same sites.

Haemangiopericytomas are tumours of the contractile cell of the capillary. They are sometimes malignant. Microscopically they are composed of numerous capillaries surrounded by masses of tumour cells. An extremely cellular lesion of the uterus which contains numerous capillaries should suggest the diagnosis. The authors present a case.

Haemangioendotheliomas are usually malignant and metastasize early through the blood stream. Stout (*Ann. Surg.*, 1943, **118**, 445) states that two criteria are necessary for the diagnosis: "First, the formation of atypical endothelial cells in greater numbers than are required to line the vessels with a simple endothelial membrane. Second, the formation of vascular tubes with a delicate framework of reticulum fibres and a marked tendency to anastomose." They are very rare.

Lymphangioendotheliomas are the lymphatic counterpart of the above.

Fibromata angiomatosa are potentially malignant tumours of the uterus. They are composed of innumerable arteries with interspersed tumour cells.

Brandfass and Scheffey present a case of haemangioma of the cervix.

J. G. Dumoulin

131. **Investigation of Urinary Steroids in a Case of Carcinoma of Adrenal Cortex Revealed by a Vaginal Mestastasis.** (Etude des stéroïdes urinaires dans un cas de carcinome cortico-surrénale découvert par une métastase vaginale.)

By R. Devis, R. Vanek and J. Ferin. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 272–293. 1955. 3 illus. 9 figs. 25 refs.

This is a study of an androgenic carcinoma of the adrenal cortex in a 26-years-old woman. The diagnosis was made by section of a vaginal metastasis. A tumour weighing 700 g. was removed. The histology of the metastasis and the original tumour is described.

The urinary steroids were studied before, and 19 days and 4 months after, the operation. The different techniques are described including a new micro-technique for the chromatographic fractioning of the 17-ketosteroids and of the alpha-pregnandolones.

The authors also discuss their own results with Allen's method for the estimation of the dehydroepiandrosterone; the results are not correct unless this author's formula is modified. The new formula gives values which are in very close agreement with those obtained by application of the Zimmerman reaction after chromatography.

The significance of the chemical procedures used here for the diagnosis is discussed. The fractionation of 17-ketosteroids is likely to give the most valuable results.

According to the authors an adrenocortical tumour can show two different types of chemical reactions, which supports the hypothesis of one of the authors about the twofold physiological potentiality of the adrenal cortex.

From the Authors' Summary

132. **Calcification in Uterine Fibromyomata.** (Sulla calcificazione dei fibromiomi uterini.)

By A. Migliavacca. *Ann. Ostet. Ginec.*, **77**, 331. Apr. 1955. 4 figs. 73 refs.

The clinical and anatomico-pathological features of calcification in uterine fibroids are considered with reference to four cases. It is concluded that calcification in fibroids is preceded by necrosis which facilitates the deposition of calcium salts in the tumour.

Josephine Barnes

133. **Cancer of the Womb, 1930–1945: Treatment Results at the King George V Memorial Hospital, Royal Prince Alfred Hospital, Compiled December 31, 1954.**

By H. Schlink. *Med. J. Aust.*, **2**, 260–261. Aug. 13, 1955. 5 tables. 1 fig.

The routine use of combined treatment with radium and surgery for carcinoma cervicis uteri has been continued. All patients received one application of radium (7,000 milligramme-hours) followed 5 to 6 weeks later by Wertheim's radical hysterectomy whenever possible. Those patients considered unsuitable for operation were treated by further radiotherapy.

The operability rate was 52·3 per cent. Of the 1,208 patients suffering from cervical cancer who were examined with a view to treatment the operative mortality rate was 3·5 per cent. For the last 10 years this has fallen to less than 1 per cent.

The five-year survival rate of all patients seen was 35·7 per cent. Of those treated with combined radium and surgery the five-year survival rate was 58·6 per cent. The ten-year survival rate of all patients seen was 25·8 per cent and of those treated with combined radium and surgery was 45·5 per cent. Patients with adenocarcinoma, and those with invaded lymph glands have a poorer chance of survival than patients with squamous malignant disease of the cervix without gland involvement.

With carcinoma corporis uteri the survival rate of all patients examined with a view to treatment was 55·5 per cent for 5 years and 45·9 per cent for 10 years. For those patients treated by the application of radium and surgery or surgery alone the five-year survival rate was 69·1 per cent.

S. Devenish Meares

134. **Ten Thousand Vaginal Smears in the Private Practice of Gynecology.**

By M. S. Allan. *Obstet. Gynec.*, **6**, 482–486. Nov. 1955. 1 ref.

Ten thousand examinations (20,000 slides) were made on smears from 5,949 patients over a period of 6 years. They were classified according to the Papanicolaou method. In 230 (3·9 per cent) the smears were "suspicious", and in 53 (0·9 per cent) were thought to be positive for carcinoma. In the suspicious class, 16 patients developed positive smears in repeat biopsies over a period of from 2 to 36 months.

In the total series 45 patients had proved malignancy, 39 of them having positive smears (accuracy rate 86·7 per cent). Five of the other 6 had suspicious smears. Among the patients with proved malignancy, 26 had carcinoma of the cervix, 17 of them early (Stage 0 or Stage I), and 18 had carcinoma of the endometrium.

Nine cases were followed up who had positive smears but no malignancy—"false-positives"—due to endometrial hyperplasia or marked epidermidization of the cervix.

J. G. Dumoulin

135. **Evaluation of 13,797 Routine Cervical Smears in a Cytology Centre.**

By W. S. Rogers, J. E. Ayre and B. Millar. *Obstet. Gynec.*, **6**, 487–492. Nov. 1955. 32 refs.

This report analyzes 13,797 routine smears during the year 1953. Cervical cell scrapings with an Ayre spatula were used. There were 435 cases graded in the pre-cancer cell complex and in atypical or malignant groups. Subtracting the 16 cases that were known treated carcinomas, there were 419 (3 per cent). Of these 214 (1·5 per cent) were in the pre-cancer group, 162 (1·2 per cent) in the malignant group, and 43 (0·3 per cent) in the suspicious group.

In the malignant group 22 per cent of the cases had cervices which looked clinically benign: the figure was 41 per cent in the suspicious group. A malignant lesion was evident clinically in only 21 per cent of the cancer group, the remainder being described as having inflammatory changes or erosions.

The authors use a ring biopsy in the suspicious and

atypical cases, believing that single biopsies are inadequate to confirm a pre-clinical lesion. They also maintain that multiple blocks and serial sections of the suspicious blocks must be done. There was quite a variance between cytological and histological findings, and in such cases repeated observations are necessary.

J. G. Dumoulin

136. **Tampon Method for Mass Screening to Detect Carcinoma of Cervix Uteri.**

By M. J. THORNTON. *J. Amer. med. Ass.*, **159**, 1177–1180. Nov. 19, 1955. 1 fig. 2 refs.

This new method of cytological detection of carcinoma of the cervix was first described by Draghi, who devised the original cotton tampon partially encased in nylon for the purpose. Brunschwig and Papanicolaou reported favourable results by this method used in 227 patients. The author of this paper reports a further large scale trial in 2,059 patients examined at the University Hospitals, Madison, Wisconsin.

The patients screened by this method were (1) clinic and private patients; (2) patients referred by other hospital departments; and (3) gynaecological clinic tumour patients, many of whom were known to have had a malignant neoplasm in the pelvis. The insertion of the tampons was supervised by a nurse in the hospital patients, but many of the out-patients group became familiar with the technique and were soon able to insert the tampons without supervision. Seven hundred and fifty-eight patients had the tampon left in the vagina overnight and 1,301 patients had the tampon left in only 10–45 minutes. The smear was made both from the end of the cotton and from the side rubbed on a Papanicolaou slide and fixed in the usual way.

In the entire group 1·2 per cent had smears with the report "malignant cells present", 0·3 per cent were "suspicious", 1·36 per cent were "unsatisfactory", and 1·36 per cent had the report "Trichomonas present". Many of the positive smears were from cases of known carcinoma. During the interval of time over which the study was made 147 of the 2,059 patients had a curettage and/or biopsy of the cervix done because of the presence of pelvic pathology. In this group of 147 patients the cytological report on the tampon smear agreed with the biopsy in 90·5 per cent, but 7·48 per cent of these 147 patients had negative smears with a positive biopsy. The Draghi detection tampon is a satisfactory method of obtaining smears, but the final diagnosis must still rest upon thorough gynaecological examination and biopsy.

D. W. James

137. **Early Diagnosis of Cancer of the Cervix Uteri.**

By M. DONALDSON. *Brit. med. J.*, **2**, 1081–1083. Oct. 29, 1955.

There may be terrible delay in visiting a doctor after a symptom of carcinoma of the cervix is noted. This is because the common initial symptoms of irregular vaginal bleeding (67·5 per cent of cases) and vaginal discharge (20 per cent) so often arise from trivial and transient causes, and women, particularly during the menopause, accept them as being "normal".

The significance of this delay is studied. Figures presented show that the prognosis is adversely affected by delay of from 3 to 6 months. There is an apparent improvement in prognosis when delay extends between 6 and 12 months but this is fallacious, for a "selection by death" has occurred of those patients with rapidly growing tumours who are eliminated from this group. Hardly any figures have been published which correlate duration of delay with stages of disease. There would probably be an increase in the number of Stage I cases if delay was cut down, and certainly Stages I and II combined would exceed Stages III and IV, but the distribution would still be over all four Stages. There is evidence from Canada, and to a limited degree from Yorkshire, that cancer education does result in treatment at an early stage of disease. The alternative—periodic overhauls—is considered by the author to be an impracticable ideal.

On the question of diagnosis, emphasis is laid on careful history taking. All patients complaining of irregular bleeding must be considered as cancer cases until this is disproved. Clinical examination must be complete and not limited to the pelvic organs. Cytological examination by the smear technique is of great value as an aid to early diagnosis, but "false negative" reports, the incidence of which may be as high as 10 per cent, may give rise to false assurance. Colposcopy too is a valuable diagnostic aid, but the Schiller iodine test cannot be relied on.

Early diagnosis will produce more early stage cancers and is essential if the best results in the treatment of carcinoma of the cervix are to be obtained.

R. W. Grayburn

138. **The Diagnosis of Malignant Tumours of the Ovary.**

By V. V. GAMPER. *Sov. Med.*, **9**, 29–34. Sept. 1955. [In Russian.]

In the Ukrainian Radiological and Oncological Institute there has been an increase in the incidence of malignant ovarian tumours in recent years, as compared with the total of malignant tumours of the female genital organs. In the years 1944–1948 there were 2–3 per cent ovarian tumours; in 1952–1953, 8–10 per cent. In the last 10 years 203 women came to the clinic with malignant ovarian tumours, classified as follows: Papillary carcinoma 42, adenocarcinoma 19, papillary adenocarcinoma 48, squamous-celled 2, sero-anaplastic 2, teratoblastoma 4, granulosa-celled 12. The remainder were diagnosed only by cytological examination of needle punctures of the tumour, or histological study of affected parts of the omentum removed at laparotomy. One hundred and thirty-five of the women were aged 40–60, so that cancer of the ovary is chiefly a disease of the pre- and post-climacteric period. One hundred and seventy-seven of the patients were in Stages 3 or 4, a very high percentage of late diagnoses. This is partly due to the lack of early symptoms, and partly to delay in diagnosis and treatment. Seventy-seven per cent came to the Institute within two months of the appearance of symptoms, but

a correct diagnosis had only been made in 11 per cent of the total number.

From these tragic figures the author reaches the following conclusions: (1) In view of the difficulties of early diagnosis of ovarian cancer, regular oversight of women in the years near the climacteric is essential. (2) All women of this age group thought to be suffering from chronic pelvic inflammatory disease must be carefully investigated, and physiotherapy involving heat should be given only after exclusion of any possibility of a neoplasm, since it may accelerate the growth. If treatment of chronic infection is not effective within two months, and any tumour is found in the pelvis, all treatment with heat should be stopped. (3) Every case of ovarian tumour, even if regarded as malignant, should be considered for surgical treatment. It should be remembered that every fourth or fifth ovarian tumour is malignant, and therefore removal of all tumours is essential. (4) In view of the difficulty of early diagnosis radiological and cytological (needle puncture and vaginal smears) methods should be employed in any case in which laparotomy is not possible. Vaginal smears are of value in estimating the oestrogenic saturation of the patient, which is increased in certain feminizing tumours. (5) Primary sterility was present in 15·5 per cent, and secondary sterility in 27·5 per cent, of this series of patients. Such a history should be in itself a ground for a suspicion of malignancy.

[The proportion of malignant to benign tumours of the ovary given in this article is much the same as that of most observers in this country. Many granulosa-cell tumours are regarded as benign. Needle puncture seems a most uncertain method of histological diagnosis in a type of tumour in which malignancy is so often localized at first to one portion of an originally benign growth. No reference is made to metastatic tumours, which form 15 per cent of all ovarian cancers.]

L. Firman-Edwards

139. **Carcinoma of the Ovary: 286 Cases Treated at the Women's Clinic, University of Helsinki, 1934-1948.** By A.-L. ALHA and L. MERENMIES. *Ann. chir. gynaec. fenn.*, **44**, 157–169. 1955. 2 figs. 16 refs.

Of 286 cases 190 were treated surgically, and 96 were considered inoperable. The average age was 52·3 years and 18·1 per cent were sterile. The main symptoms were abdominal pain and gastrointestinal troubles. 65·6 per cent were treated within six months of the onset of symptoms. Only 32·6 per cent showed ascites and 46·8 per cent showed metastases. Ten per cent were associated with fibroids. The 5-year cure rate of all cases subjected to operation was 36·3 per cent. With total hysterectomy and bilateral salpingo-oöphorectomy a 5-year cure rate of 64·3 per cent was obtained; with subtotal hysterectomy only 41·4 per cent. The cure rate is only very slightly better when deep X-ray therapy is given as well. Of the inoperable cases 62 received X-ray treatment and 34 no treatment. With X-rays the 5-year cure rate was 12·9 per cent. With no treatment the 5-year cure rate was 14·7 per cent. However none of these cases were confirmed histologically. *D. M. Sheppard*

140. **A Review of 306 Cases of Endometrial Carcinoma.** By H. B. BOURNE, J. P. A. LATOUR and N. W. PHILPOTT. *Surg. Gynec. Obstet.*, **101**, 753–758. Dec. 1955. 5 figs. 8 refs.

The review embodies the 306 cases of endometrial carcinoma met with at the Royal Victoria Montreal Maternity Hospital during the years 1926 to 1953 inclusive. An apparent increase in the number of cases in the latter years is explained by a greater turnover in the gynaecology department and by a general increase in the life span of women.

It is interesting to note that 43 of the patients were still menstruating after the age of 52 years and that 32 or 10·5 per cent of the total had diabetes.

All were adenocarcinomas and only a few showed acanthomatous change. The value of cytological examination of the vaginal pool contents in the detection of endometrial carcinoma is discussed and its accuracy is found to be in the neighbourhood of 65–70 per cent.

Treatment is considered fully and the authors report an absolute 5-year cure rate for the period 1926–1948 inclusive of 59·3 per cent. Of the patients treated by surgery, 69 per cent survived 5 years or longer, while of those treated by radium, the 5-year survival rate was 52·9 per cent. It is accepted that in some ways the comparison is unfair as radiation therapy has been employed mainly in cases considered unsuitable for surgery and the radiotherapeutic technique employed has not been ideal. However, the authors are convinced that surgical extirpation of the pelvic genital organs offers the best chance of effecting a permanent cure.

John P. Erskine

OPERATIONS

141. **A New Approach to Operations for Prolapse.** By J. C. LOXTON. *Med. J. Aust.*, **2**, 444–448. Sept. 17, 1955.

Following the Manchester operation the author has found poor results such as an appreciable number of recurrences, the development of enterocele, narrowing of the vagina, cervical stenosis, and the retention of an unhealthy uterus. Recurrence of the original prolapse is as much the fault of the operator as it is of the failure of the technique of the operation itself.

The occurrence of an enterocele is due to the shortening of the anterior vaginal wall moving the cervix forward so exposing the weak posterior part of the pelvic floor. Something more than the Manchester operation is required to support the bladder neck. The narrowing of the vaginal vault is due to the skin still attached to Mackenrodt's ligaments being sutured in front of the cervix. So as not to narrow the vagina the author refrains as far as possible from removing any vaginal skin at all The vaginal skin at the end of the operation sometimes has a ravelled up and creased appearance but by the time healing is complete this redundance is no longer apparent.

The operation of vaginal hysterectomy and repair avoids many of the pitfalls of the Manchester operation. In the absence of the uterus Mackenrodt's and the

utero-sacral ligaments can be more securely united and shortened, and an opportunity is afforded to increase the length of the vaginal canal. When it is decided not to remove the uterus, the operation proceeds as for vaginal hysterectomy, stopping short of the ligation and division of the uterine arteries. Mackenrodt's ligaments and the utero-sacral ligaments are ligated and their attachments to the uterus divided, the stumps being united and sutured to the front of the cervix. When the uterus is removed abdominally Mackenrodt's ligaments and the utero-sacral ligaments are united in the mid line above the vaginal vault. *S. Devenish Meares*

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